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Effect of Mephenesin Alone and in Combination with Pentobarbitone Sodium on Consciousness and Appreciation of Pain

BY

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SUMMARY.—The effect of mephenesin, alone, and in combination with pentobarbitone sodium, has been studied in rabbits. This has been done by direct observation and by recordings of electrical activity from the cerebral cortex and spinal cord. The mixture of pentobarbitone sodium and mephenesin marketed as Pentolissin is not likely to produce paralysis without unconsciousness. The 2 drugs act synergistically on the brain, and mephenesin could not necessarily be mixed successfully with other anaesthetics to produce muscular relaxation. Mephenesin itself acts on the brain, not simply on the spinal cord as has often been supposed. It has no analgesic activity, but is, in fact, likely to facilitate transmission of pain impulses to the cerebral cortex. Intravenous injection of Pentolissin in the rabbit often causes thrombosis; this may be due to the solvent or to the high concentration of mephenesin.*

Introduction

PENTOLISSIN is a solution containing 1 gr. pentobarbitone sodium and 0.5 gr. mephenesin per ml. and is described by the makers as being a particularly useful anaesthetic agent for operations which require increased muscular relaxation; it is stressed that the relaxant activity of mephenesin in the solution is not similar to that of a curariform drug which acts at the neuromuscular junction, but is exerted at a central site. Apart from its relaxant properties, Pentolissin is also said to produce a quicker return to consciousness after general anaesthesia than pentobarbitone sodium alone, and hence to reduce the time during which an animal need be kept under supervision on a veterinary surgeon's premises after an operation.

Although mephenesin acts centrally, there is no suggestion from previous work that it has any effect on consciousness. The pentobarbitone sodium in Pentolissin is, presumably, wholly responsible for producing unconsciousness, while the mephenesin provides additional relaxation. If this is so, it would not be possible for a veterinary surgeon, who normally judges anaesthetic level by lack of muscular reflexes, to know whether the limpness and lack of response in the animal were due to unconsciousness, or to relaxation and paralysis by mephenesin. In human medicine there are now a number of reports of surgery having been performed on patients who were conscious but under the influence of a relaxant (Clark, 1956; Shea, 1954; Winterbottom, 1950).

Pentolissin, as supplied by the makers and used on the normal animal, is obviously calculated to provide adequate loss of consciousness in addition to relaxation, but there are 2 contingencies in which this might not occur: (1) if the pentobarbitone activity of the mixture had deteriorated relative to the mephenesin activity; this is a real possibility because barbiturate solutions do deteriorate with time if stored under unfavourable conditions; (2) if the animal were unduly resistant to pentobarbitone sodium as an anaesthetic agent. Animals of the same species, or even the same animal at different times, do vary considerably in their reaction to barbiturate (Table I). This is more noticeable with some preparations of pentobarbitone sodium than others, and may depend on the solvent or on substances used to keep the barbiturate in solution.

* Allen & Hanbury, Ltd.

TABLE I

VARIABILITY OF RESPONSE TO PENTOBARBITONE SODIUM IN THE RABBIT

No.	Rabbit	Weight (lb.)	Barbiturate preparation	Dose (gr. per lb.) (B.W.)	Level of anaesthesia
1	Biddie	8·0	Nembutal	0·08	Very light
2	,,	8·0	,,	0·08	,, ,,
3	21/24	6·5	,,	0·12	,, ,,
4	21/24	6·5	,,	0·18	Surgical
5	Loppy	5·2	Sagatal	0·20	Light
6	Patch	7·0	Nembutal	0·22	Surgical
7	Sally	7·0	,,	0·22	Light
8	Tiny	5·2	,,	0·22	,,
9	Chubby	9·0	Sagatal	0·22	Very deep needing artificial respiration
10	Sally	7·0	Nembutal	0·22	Surgical
11	22/24	5·2	,,	0·24	,,
12	24/24	5·7	,,	0·24	,,
13	Patch	7·0	,,	0·24	,,
14	Peter	6·0	,,	0·24	,,
15	Biddie	8·0	,,	0·24	,,
16	Patch	7·0	,,	0·24	,,
17	Topsy	6·0	,,	0·24	,,
18	23/24	4·7	,,	0·26	Very deep needing artificial respiration
19	Chubby	9·0	Sagatal	0·28	Surgical
20	Tiny	5·2	,,	0·28	,,
21	19/24	4·7	Nembutal	0·30	,,
22	Charlie	8·5	Sagatal	0·30	Very deep needing artificial respiration
23	Peter	6·0	Nembutal	0·32	Surgical
24	Rex	6·2	Sagatal	0·32	Very light
25	Loppy	5·2	,,	0·34	Light
26	Grey	6·5	,,	0·34	,,
27	Rex	6·2	,,	0·36	Very light
28	Charlie	8·5	,,	0·36	Light
29	Patch	7·0	,,	0·36	Surgical
30	Patch	7·0	,,	0·36	Light
31	Loppy	5·2	,,	0·38	Very deep needing artificial respiration

The reason for the second characteristic property of Pentolissin given by the makers—quicker recovery after general anaesthesia—is not immediately obvious on physiological grounds, because the recommended dose of Pentolissin involves injection of the same amount of pentobarbitone sodium as if straight barbiturate anaesthesia were being used. Apparently, the addition of a centrally acting relaxant, mephenesin, reduces the duration of the effect of a barbiturate on consciousness. Curariform relaxants, acting peripherally, do allow quicker recovery from anaesthesia in many cases because they allow the surgeon to use a smaller dose of anaesthetic; but with Pentolissin the recommended anaesthetic dose is not reduced. This suggests that there is synergism between pentobarbitone sodium and mephenesin when injected together in Pentolissin. The experiments described in this paper were carried out in an attempt to understand better the action of mephenesin in Pentolissin, and to investigate the likelihood of paralysis without unconsciousness occurring, if Pentolissin were used carelessly.

Experimental Material

The experimental animals were full-grown rabbits of both sexes, varying between 4.7 and 9.0 lb. in bodyweight. In veterinary practice Pentolissin is normally used for dogs and cats; rabbits were used in these experiments because, while their brains and central nervous systems are essentially similar to those of dogs and cats, they are more convenient to maintain and handle.

Experimental Procedure

The electrical activity of brain and spinal cord was recorded on a standard Ediswan 2-channel portable EEG machine. The cortical electrodes were similar to those of Bradley and Elkes (1953) except that platinum wire was used instead of silver because silver wire broke too easily at the point where the wire emerged from the screw-holder. The cortical electrodes were inserted, one on each side of the skull, 0.1 inch lateral to the mid-line, half-way between the posterior canthus of the eye and the anterior point of attachment of the base of the ear. *Post-mortem* examination showed that, using these external landmarks, the electrode tip was always near the junction of the middle and posterior thirds of the cerebrum. Stereotactic placing was not found necessary, because the so-called alpha rhythm (Fig. 1) and the response to sensory stimuli could always be recorded from electrodes inserted with the aid of these external landmarks.

The electrodes for recording from the spinal cord were stainless steel hypodermic needles (B.W.G. 22 or 23), insulated with shellac except for a bared tip, and inserted between the third and fourth, and fourth and fifth, lumbar vertebrae. They were pushed down very gently until there was a characteristic flick of the rabbit's tail indicating that the spinal cord had been touched. These electrodes were removed at the end of each day's experiment, so that *post-mortem* examination of the exact location was not carried out. The earth lead was clipped to a stainless steel hypodermic needle placed subcutaneously on the rabbit's back.

The cortical electrodes caused no disturbance to the conscious animal, and could be left in position for weeks without affecting its normal habits in any way. Electro-corticograms showed no evidence of injury to the brain, and *post-mortem* examinations confirmed that tissue reaction was negligible in the vicinity of the electrode.

The stimulus for assessment of reaction to pain was a pin-prick in the upper part of the hind leg. Pentolissin itself was not used in the later experiments because it caused marked venous thrombosis and gangrene in the rabbits' ears when injected intravenously. The requisite volume of a 1 per cent. solution of mephenesin in normal saline was added to pentobarbitone solution so as to simulate Pentolissin. This solution caused no trouble at the time of injection or afterwards. All injections were made by the same experimenter and frequent checks showed that the rate of injection was between 15 and 20 seconds per ml.

Cross-over experiments, using unknown drugs,

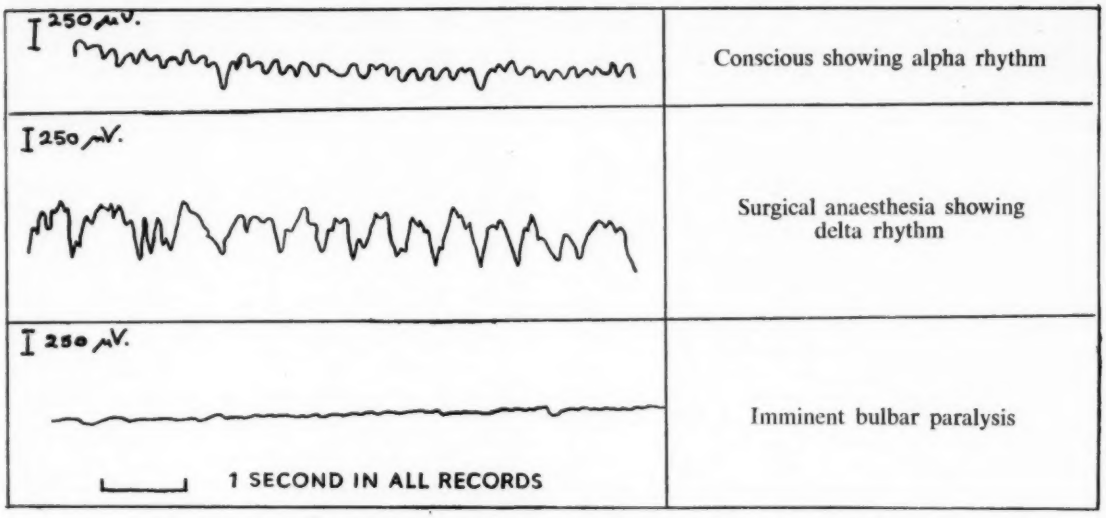

FIG. 1.—Electro-corticogram of Rabbit at Different Levels of Consciousness.

were not easy to arrange but certain precautions were taken to prevent prejudiced assessment of results. The time taken to reach the various stages of recovery was frequently noted by a technician who was unaware of the significance of the whole research scheme. Comparable experiments with pentobarbitone sodium and Pentolissin were not normally done on consecutive days, so that times of recovery were not remembered. Electro-corticograms were frequently studied blind, weeks after the actual experiment, and any records which then seemed doubtful were discounted.

Levels of deepening anaesthesia were defined as follows: *very light*—rabbit loses ability to stand, but will not remain lying on side if placed in that position; *light*—rabbit loses ability to stand and will remain on side if placed there; *surgical*—hind-leg retraction reflex, negative, and palpebral reflex slowed; *deep*—hind-leg retraction and palpebral reflexes negative. Points for comparison of recovery times were as follows: (i) rabbit attempts to rise from lateral recumbency without external stimulus; (ii) rabbit can maintain natural crouched sitting position; (iii) rabbit makes spontaneous attempts to hop on laboratory floor, but is still inco-ordinate; (iv) rabbit hops normally and takes an interest in surroundings. Points (ii) and (iv) were surprisingly sharp and could be timed to within 2 or 3 minutes. These external signs were used in conjunction with electro-corticograms to assess stage of recovery.

Results

1. *Variability of dose of pentobarbitone sodium necessary to produce given depth of anaesthesia*

The depth of anaesthesia was assessed as described above, and in the absence of relaxants there was no significant difference between the results from clinical signs and from electro-corticograms. Table I shows that the dose needed to produce surgical anaesthesia is extremely variable from one rabbit to another, and in the same rabbit at different times. Thus in No. 9, 0.22 gr. per lb. bodyweight produced anaesthesia so deep as to need artificial respiration, whereas in No. 27, 0.36 gr. per lb. bodyweight produced very light anaesthesia. Again, in No. 22, 0.30 gr. per lb. bodyweight produced very deep anaesthesia needing artificial respiration on one occasion, while 2 weeks before, in the same rabbit, 0.36 gr. per lb. bodyweight (No. 28) failed to produce surgical anaesthesia, and ether was necessary to supplement the barbiturate anaesthesia.

TABLE II
DEPTH OF ANAESTHESIA INDUCED BY VARYING DOSES OF PENTOLISSIN

No.	Rabbit	Dose		Level of anaesthesia
		ml. pentolissin per lb. bodyweight	gr. barbiturate per lb. bodyweight	
1	Grey	0·12	0·12	Slight sedation
2	Loppy	0·17	0·17	Light
3	Grey	0·18	0·18	„
4	Loppy	0·19	0·19	Deep, needing artificial respiration
5	Chubby	0·22	0·22	Surgical
6	Charlie	0·24	0·24	Light
7	Patch	0·28	0·28	Deep
8	Charlie	0·30	0·30	„

2. *Effect of Pentolissin*

a. *Depth of anaesthesia.* The results of Table II show that, bearing in mind the wide variation in response shown in Table I, Pentolissin produces that level of anaesthesia which would be expected from the barbiturate content of the solution. There is no evidence to suggest that the relaxant activity of

mephenesin in the solution causes loss of reflexes while the animal is still conscious. In No. 2, for instance, where the state of consciousness as indicated by the electro-corticogram was that of light anaesthesia, the reflexes were positive and indicated the same depth of anaesthesia.

b. *Duration of anaesthesia.* Table III shows that, with one exception (No. 8), recovery from similar depths of anaesthesia occurs more rapidly when the anaesthesia has been produced by Pentolissin than when it is due to pentobarbitone sodium alone. This occurs when the animal has received the same dose of barbiturate by each method, and the increased speed of recovery must therefore be associated with the mephenesin content of Pentolissin. This accelerated recovery rate was noticeable from 10 minutes after induction onwards, and was shown equally in electro-corticogram records and in reflex activity. The one exception in Table III (No. 8) was a rabbit which was extraordinarily resistant to barbiturate anaesthesia; dosage of 0.36 gr. per lb. bodyweight only produced light anaesthesia, and the recovery in this animal was not from truly comparable states of anaesthesia.

TABLE III

COMPARISON OF RECOVERY TIMES AFTER PENTOLISSIN AND BARBITURATE ANAESTHESIA

No.	Level of anaesthesia	Time taken to reach same stage of recovery (minutes after induction)	
		Induction with pentolissin	Induction with barbiturate
1	Light	15	40
2*	Surgical	65	85
3	,,	65	90
4	,,	65	90
5*	Deep	20	45
6	,,	25	40
7	,,	15	50
8	,,	45	25

NOTES.— (1) The comparison was not made at the same point in the return to consciousness in the 8 experiments ; the accelerated recovery after pentolissin can be detected from 10 minutes after induction onwards, so that it is immaterial whether comparisons are made at 10, 25 or 60 minutes.

*(2) These rabbits were again anaesthetised some weeks later with pentobarbitone sodium, and the repeat experiment showed a similar recovery time in both animals.

3. *Effect of mephenesin*

a. *Alone.* Mephenesin was injected as a 1 per cent. solution in normal saline. When injected in the dosage in which it would be given for surgical anaesthesia in Pentolissin (0.1 gr. per lb.) this had no effect whatever on reflexes or behaviour. A minimum dose of 0.2 gr. per lb. was necessary to produce any effect, and in many rabbits there was no obvious change until about 0.35 gr. per lb. was given. Typically, then, there was momentary relaxation followed by extreme stiffness which was most marked in the hind legs, and persisted for about 20 seconds. This was followed by some degree of relaxation. The rabbit usually got up after about 10 minutes, and could then hop about, but some inco-ordination of the hind quarters was often seen up to 70 minutes after the injection. The typical head-drop described in the British Pharmaceutical Codex was only seen once, with a dose of 0.2 gr. per lb. bodyweight. The same rabbit did not show it when the experiment was repeated a few days later. Rabbits injected with mephenesin usually lost the hind leg reflex for a few minutes after injection, but the palpebral reflex always remained positive. This confirms the observations of Berger and Bradley (1946) on reflexes. The inhibition of the hind-leg reflex seemed to be due to stiffness rather than to paralysis or flaccidity.

b. *In conjunction with pentobarbitone sodium.* If mephenesin was given some time after an injection of barbiturate, as the anaesthesia was lightening, the normal return to consciousness was somewhat delayed ; if it was given at the same time as the barbiturate, recovery was accelerated. In neither case was the dosage critical, and the amount of delay or acceleration was not proportional to the dose of mephenesin. There was no evidence that, if mephenesin was present in excess, as it might be if Pentolissin had deteriorated during storage, it would produce paralysis which might be mistaken for unconsciousness. Under all conditions, the state of the animal as assessed by the electro-corticogram agreed with that shown by palpebral reflex activity.

4. *Electrical activity*

The conscious electro-corticogram of the rabbit has been described now by many workers; it can be analysed into components of various frequencies, and the dominance of a particular frequency is usually an indication of the state of consciousness of the animal (Fig. 1). The electro-corticogram of a normal conscious rabbit shows a dominant frequency of 4 to 7 c./s. As the rabbit loses consciousness this so-called alpha rhythm of 4 to 7 c./s. disappears, and when the animal reaches the stage of surgical anaesthesia, the electro-corticogram consists mainly of a rhythm of 1 to 3 c./s., the so-called delta rhythm. When bulbar paralysis is imminent, even the delta rhythm goes and the electro-corticogram is almost flat. As anaesthesia lightens these changes are reversed and the alpha rhythm reappears as the rabbit regains consciousness.

In these experiments the records showed all the usual features. Alpha rhythm was always present in the conscious electro-corticogram and was used as a criterion of returning consciousness after general anaesthesia. It coincided with the animal's first attempts to hop, and with its ability to maintain the normal crouching position.

a. *Effect of pentobarbitone sodium.* The changes in the rabbit electro-corticogram due to barbiturate anaesthesia are also well-known and are comparable with those seen in the human. In these experiments the typical changes occurred regularly; light, surgical, and very deep anaesthesia could be readily distinguished by electro-corticogram alone. The effect of barbiturate on the spinal cord record (cordogram) was not very marked; the principal feature was irregular spiking in the record during the period of anaesthesia.

b. *Effect of Pentolissin.* In general the effect of Pentolissin on the electro-corticogram was similar to that of barbiturate alone, but there was also evidence of some increase in the voltage of the alpha rhythm when the plane of anaesthesia was very light. Pentolissin had little effect on the cordogram.

c. *Effect of mephenesin.* Mephenesin caused an increase in the voltage of the cortical alpha rhythm, and a slight slowing of this rhythm, so that the frequency was in the range 3 to 5 c./s. instead of 5 to 7 c./s. The increase in the voltage was often slight, but it always occurred; in the one case in which head-drop was seen, the increase in the voltage was startling, being about five-fold. The effect usually lasted 7 to 13 minutes and was not directly dependent on dosage, since it appeared with all doses between 0.1 and 0.4 gr. per lb. to the same extent. The marked effect seen with head-drop followed a dose of 0.2 gr. per lb.; the increased voltage ceased to be continuous at 7 minutes after the injection, precisely at the moment when the rabbit tried to get up, but the electro-corticogram was not entirely normal until one hour after injection.

Occasionally, slow waves were seen in the electro-corticogram after administration of mephenesin, similar to those described by Last and Weil-Malherbe (1950), but these seemed dependent on injection of barbiturate earlier in the day. Normally, if barbiturate had been injected in the morning, no other drugs would be given during the afternoon. The foregoing observations were made during pilot cordogram experiments when spinal electrodes were being inserted under very light barbiturate supplemented by local anaesthesia in the morning, and recordings attempted in the afternoon, since permanent spinal electrodes proved difficult to implant. When it was realised that pentobarbitone sodium might be confusing the later results, the technique was changed and ether was used as anaesthetic for implantation. Once, after a very small dose of mephenesin (0.12 gr. per lb.), slight flattening of the alpha rhythm of the electro-corticogram was seen, but this effect was not repeatable.

Effects on the cordogram were, in general, less marked, but there was usually some flattening and suppression of fast frequencies in the spinal cord, coincident with the increase in voltage and slowing in frequency of the electro-corticogram. On one occasion mephenesin (0.26 gr. per lb.) produced a striking cordogram of continuous high-voltage sharp waves for 15 minutes after injection; there was no concurrent disturbance in the electro-corticogram.

d. *Transmission of pain impulses after administration of drugs.* When anaesthesia was induced by pentobarbitone sodium alone, or by Pentolissin, stimuli applied at the hind leg appeared as spikes on the cordogram but could not be detected on the electro-corticogram. When mephenesin alone was injected in doses varying from 0.02 to 0.20 gr. per lb., the stimuli applied to the hind leg appeared at the cortex on the electro-corticogram as spikes of slightly higher voltage than before injection. This enhancement of registration of pain at the cortex persisted up to 6 minutes after the injection, and was not proportional to the dose. Sometimes, as well as the increased voltage of a single spike, there was a spiky after-discharge on the electro-corticogram lasting up to 20 seconds from the original stimulus. When mephenesin was injected as barbiturate anaesthesia was becoming lighter, or at the same time as a dose of barbiturate sufficient only for very light anaesthesia, this enhanced registration of pain at the cortex did not appear.

There was no gross disturbance of respiration or heart-rate as judged by the usual clinical procedures of observation and palpation in any of these experiments. Bruising and thrombosis at the site of injection were serious with Pentolissin, and occurred to a lesser degree with some preparations of pentobarbitone sodium. The trouble disappeared entirely when weaker solutions of mephenesin, in normal saline, were used and when the barbiturate solution was made up with water.

The trouble is apparently due either to the solvents or, in the case of Pentolissin, to the relatively high concentration of mephenesin (3 per cent.).

Summary of Experimental Results

1. Mephenesin increases the voltage and reduces the frequency of alpha rhythm at the cortex.
2. At the same time it decreases slightly the electrical activity of the spinal cord.
3. Pain stimuli are readily transmitted to the cortex from the periphery after an injection of mephenesin, and the response at the cortex may be somewhat enhanced in size and duration as a result of injection.
4. Mephenesin affects the postural reflexes of the rabbit, and its ability to stand and hop, but it does not produce marked flaccidity.
5. When combined with barbiturate as Pentolissin, mephenesin decreases the recovery time after general anaesthesia.

Discussion

Since the effects of mephenesin were first described by Berger and Bradley in 1946, numerous theories have been put forward about its site of action. Berger and Bradley (1946) themselves considered that it acted on the spinal cord and that it had an ascending depressant action. They based this theory largely on the fact that it antagonised strychnine convulsions, but had no effect on leptazol convulsions; strychnine convulsions were considered to originate in the spinal cord, while leptazol ones were considered to arise from the brain itself. They noted that it was synergistic with barbiturates and that narcosis resulted from an infective dose of barbiturate plus an ineffective dose of mephenesin. They reported that mephenesin had no analgesic properties.

In 1947 Stephen and Chandy used human EEGs and electrical recordings from spinal cats in an attempt to determine the site of action of mephenesin. They deduced that mephenesin (in a dosage below 0.28 to 0.35 gr. per lb.) had no effect on transmission in the spinal cord or at the neuro-muscular junction, but that it had a selective action on the extra-pyramidal system, or on the thalamus and associated

parts of the mid-brain. This deduction was based partly on clinical observation, partly on human EEGs and partly on animal experiments. These workers also found that in some patients a 10 per cent. solution of mephenesin produced thrombo-phlebitis, and in some haemolysis and haemoglobinuria. Pugh and Enderby (1947) also noted that haemolysis followed intravenous injection of mephenesin, and recommended that it should always be diluted to at least a 1 per cent. solution in normal saline.

Hunter and Waterfall (1948) found, in agreement with Stephen and Chandy (1947), that mephenesin improved Parkinsonian tremor, and central or thalamic pain, they concluded that the site of action was probably the basal ganglia other than the hypothalamus, and this idea of a central site of action was supported by their observations on circulation times. Last and Weil-Malherbe (1950), working with rabbits, found that doses of 0.17 to 0.52 gr. per lb. greatly increased the 5 c./s. activity in the rabbit EEG and suggested that this was due to an effect on sub-cortical structures. In the same year Kaada (1950), using cats and monkeys, found that multisynaptic pathways in the central nervous system were specially vulnerable to mephenesin, and that the normal facilitatory activity of the brain-stem reticular system was depressed by it.

The evidence based on the suppression of convulsions induced by strychnine and leptazol is somewhat tenuous because the effect of these convulsants on the nervous system is not simple: strychnine, for instance, may affect structures in the medulla, cerebellum, and cortex, as well as in the spinal cord. The results described in this paper are compatible with the majority of those listed above, but they do not support the finding that narcosis results from an insufficient dose of barbiturate plus an insufficient dose of mephenesin. A working hypothesis for the experimental results given here depends partly on the work of Gangloff and Monnier (1956) and Rinaldi (1958) on the origins of the rabbit electro-corticogram (Fig. 2).

Gangloff and Monnier (1956) showed that the rabbit electro-corticogram is largely dependent on two factors:—

i. Reticulo-cortical mechanism causing low-voltage fast activity.

ii. Thalmo-cortical mechanism causing alpha activity, the thalamus itself tending to have a slightly slower rhythm of 4 to 5 c./s. (alpha rhythm being 4 to 7 c./s.).

Rinaldi (1958) likewise showed that the alpha rhythm of the cortex has its origin in sub-cortical structures, especially the hippocampus. Since the present experiments have shown that mephenesin augments the alpha rhythm at the cortex, and tends to lower its frequency so that it corresponds more exactly to that of the thalamus, it seems reasonable to suppose that the drug facilitates transmission in the thalamo-cortical system (ii, above), and suppresses the activity of the reticulo-cortical system (i, above) as Kaada (1950) found in cats. The suppression of i. might be due to a direct action on the reticular system or to suppression of impulses reaching it from the spinal cord, but as the cordogram is not noticeably affected by mephenesin, it seems likely that the main effect is on the reticular system itself. The effect on posture in the rabbit, and on Parkinsonism in man suggest that the drug probably affects the extra-pyramidal tract also.

This hypothesis, which seems the simplest one

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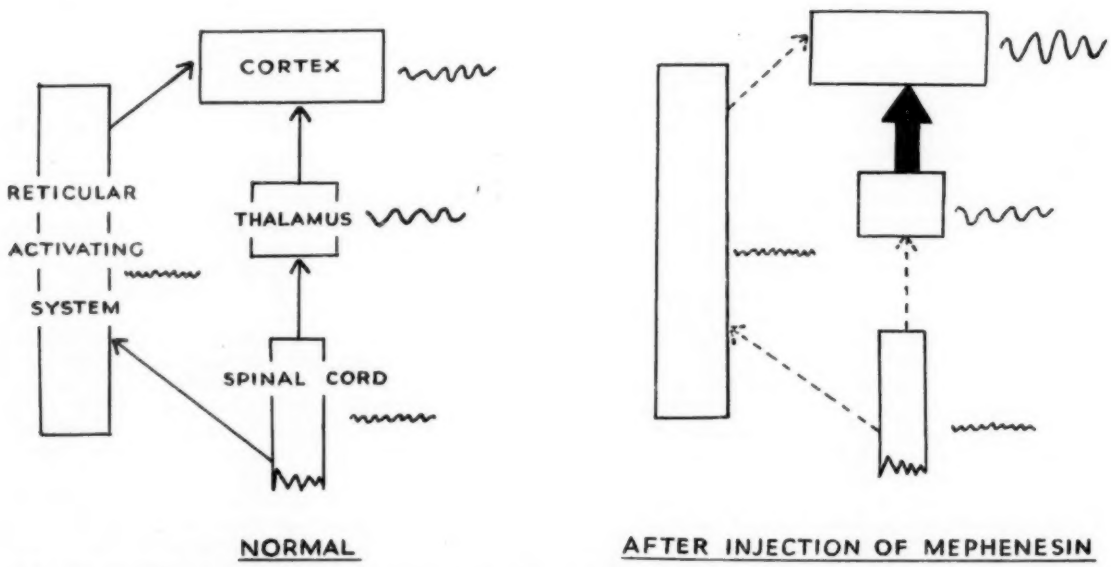

FIG. 2.—Possible sites of action of mephenesin and effects on electrical activity of brain and spinal cord of rabbit.
Note. The above is a grossly simplified diagram, and is not intended to do anything more than illustrate the hypothesis put forward in the text.

Problems Concerning Drug Resistance in Parasitic Protozoa

BY

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THE discovery that micro-organisms could be made resistant to drugs in the course of treatment of the host was made in Ehrlich's laboratory, in Germany, early in the present century. Whilst searching for synthetic compounds with which to treat trypanosomiasis of man and animals two of his colleagues, Fränke and Röhl, observed that although infections of *Trypanosoma brucei*, experimentally induced in mice, at first responded to treatment with parafuchsin, the drug gradually lost its inhibitory effect upon the trypanosomes and finally the mice died of the infection in spite of continued treatment with the drug. These trypanosomes, when inoculated into normal mice, were, from the beginning, unaffected by the drug; they had become parafuchsin-resistant. Since that early discovery, strains of trypanosomes have been made resistant, experimentally, to a wide variety of trypanocidal substances including compounds used in the treatment of trypanosomiasis in man, such as tryparsamide, suramin (Bayer, 205) and stilbamidine, and antrycide which is used in the treatment of trypanosomiasis in cattle. Moreover, resistant infections occur as a result of therapeutic treatment; thus cases of human trypanosomiasis resistant to tryparsamide are frequently encountered in the Belgian Congo, and trypanosome infections resistant to antrycide have been observed in cattle in parts of Africa where that drug is used.

Although quinine has been used in the treatment of malaria since early in the 17th century the malaria parasite has not lost its sensitivity to this drug, but during and since the Second World War its use has been to some extent superseded by that of synthetic drugs, and it has been shown that malaria parasites can be made resistant experimentally to several of these compounds, more especially to proguanil (paludrine) and pyrimethamine (daraprim). Malarial infections resistant to these compounds have been reported from certain areas where they have been used in the treatment of the disease.

The development of resistance is not always limited to the drug to which the parasites have been exposed but may extend to other compounds not

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Effect of Mephenesin Aloae and in Combination with Pentobarbitone Sodium—*Concluded.*

that can account for the electro-corticogram results, does not entirely explain the reduction in recovery time after barbiturate anaesthesia, in the presence of mephenesin. It seems, however, that increasing ease of transmission between thalamus and cortex could counteract the deadening effect of barbiturate on the cortex as soon as those cells approached the threshold of re-excitability. This would fit in with the observed facts on the electrocorticogram and with the animal's behaviour. Brazier (1958) has recently shown that barbiturates act on the sub-cortical structures as well as on the cortex; it may well be that mephenesin and barbiturate injected simultaneously as Pentolissin, act on the same part of the brain in a truly synergistic manner which cannot really be evaluated in terms of each component separately.

Conclusion

There is no reason to suppose that paralysis without unconsciousness will result from the use of mephenesin and pentobarbitone sodium in the proportions found in Pentolissin. Mephenesin alone does not have a simple action confined to the spinal cord. It probably affects a number of sub-cortical structures including the thalamus, hippocampus, reticular, and extra-pyramidal systems. It facilitates transmission of thalamic impulses to the cortex, and might well increase sensations of pain in the conscious animal; it should therefore never be used in any technique which does not involve adequate general anaesthesia. It acts synergistically with barbiturates, but cannot be assumed to behave in a similar manner if mixed with anaesthetics, such as steroid derivatives, which have a different chemical structure.

Acknowledgments.—I wish to express my thanks to Dr. R. E. Glover and to Professor E. C. Amoroso for providing laboratory, workshop, and animal house facilities for this work; also to Major C. W. Hume for helpful criticism and advice.

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necessarily resembling it in chemical structure; thus trypanosomes made resistant to the acridine compound acriflavine are likewise resistant to certain arsenical compounds such as tryparsamide, and vice versa; antrycide-resistant trypanosomes may be resistant to dimidium (Wilson, 1949; Fiennes, 1953), and malaria parasites resistant to pyrimethamine may be resistant to proguanil though this resistance is not always reciprocal. In searching for new drugs with which to treat these diseases it is therefore important to discover not only whether the drug is effective in doses well-tolerated by the host, but also whether it gives rise to resistant infections, and whether such infections, if they should arise during treatment, would be resistant to drugs which are already in use for the treatment of the disease.

The fundamental problem, and it is one which has interested workers from Ehrlich's time onwards, is what changes do organisms undergo in becoming resistant to drugs and how are these changes initiated? The problem is a more difficult one to study in trypanosomes and malaria parasites than in bacteria since no satisfactory method is known of cultivating the bloodstream form of trypanosomes indefinitely, nor can erythrocytic parasites of *Plasmodium* be cultivated for any useful period. However, it is possible to maintain the bloodstream form of trypanosomes in a viable state for 24 hours in a nutrient medium, and a beginning has been made in studying the changes which occur in these organisms when they become resistant to drugs. More than 25 years ago Yorke, Murgatroyd and Hawking (1931) found that trypanosomes resistant to certain arsenical compounds, unlike normal trypanosomes and dead arsenic-resistant trypanosomes, failed to absorb these compounds. Failure to absorb drugs is not, however, a property common to all types of drug resistance in trypanosomes; thus, more recently, Ormerod (1952) found that antrycide-resistant trypanosomes absorbed that drug.

A slightly lower rate of glucose consumption and pyruvate production was observed by von Brand, Tobie, Mehlman and Weinbach (1953) in a tryparsamide-resistant strain of *T. gambiense* as compared with the normal strain, and some distinct changes in metabolic function have been demonstrated by Williamson (1953a) in a strain of *T. rhodesiense* made resistant to melarsen, an arsenical compound; these changes comprise the loss of dehydrogenase activity towards glycerol, pyruvate, glutamate and succinate, and the appearance of dehydrogenase activity towards lactate. Also, a study of the effect of enzyme inhibitors upon normal and stilbamidine-resistant strains of *T. rhodesiense* has suggested that there are differences in the enzymes present in these strains (Williamson, 1953b). As yet the physiological changes which render malaria parasites resistant to drugs have not been explored.

Whatever the changes in an organism may be which lead to drug resistance, whether it be a change in permeability to or fixation of the drug, or a change in metabolism, or the production of a specific enzyme leading to the inactivation of the drug, the problem of the method by which resistance originates in the organism still exists. Two principal theories have been put forward to explain the origin of drug resistance in micro-organisms; according to one theory it arises by mutation, whereas according to the other it is the result of an automatic adaptive response of the cell components to the new environmental factor.

In some micro-organisms whose life-cycle includes a sexual phase, it is possible to analyse the inheritance of drug resistance by Mendelian methods or by the more recent recombination test, and thus to discover whether drug resistance is controlled by genes. In malaria parasites a sexual cycle of development occurs in the mosquito vector and is an obligatory stage in the life cycle. Bishop and Birkett (1947) and Williamson, Bertram and Lourie (1947) showed that resistance to proguanil was retained undiminished after a proguanil-resistant strain of *Plasmodium gallinaceum* had been transmitted by *Aëdes aegypti*, but the complexity of the life-cycle of this organism, and its dependence upon its hosts, makes a Mendelian analysis of the inheritance of resistance impossible. In trypanosomes no sexual cycle of development has been proved to occur. Nevertheless, certain observations suggest that drug resistance arises by mutation in these organisms. Thus, drug resistance may persist for long periods in the absence of the drug; an atoxyl-resistant strain of *T. rhodesiense* was still resistant to this compound 24 years after it had last been exposed to its action (Fulton & Grant, 1955), and no loss in resistance to proguanil was observed when a strain of *P. gallinaceum* resistant to this drug was maintained in its absence, in a state of acute infection in young chicks, for more than a year (Bishop & McConnachie, 1950). Moreover, although drug resistance normally develops in strains of trypanosomes and malaria parasites which have been repeatedly exposed to the action of the drug, a strain of *T. equiperdum* was found to have become resistant to certain arsenical trypanocidal compounds although it had not previously been in contact with any drug (Eagle & Magnuson, 1944), and, more recently, a change in sensitivity to two dihydrotiazine compounds and to sulphadiazine was observed to occur in a strain of *Toxoplasma gondii* (an organism classed with the Sporozoa) which, likewise, had not previously been in contact with the drug (Winter & Foley, 1956).

A greater knowledge of the physiology and metabolism of these parasitic organisms is, however, necessary before many interesting problems relating to their resistance to drugs can be fully elucidated.

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A Survey of the Incidence of *Mycobacterium johnei* Infection in Calves Under One Week Old

BY

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SUMMARY.—In a survey involving 158 calves under one week of age, only one was found to be infected with Mycobacterium johnei. *The significance of this finding with reference to the epidemiology of the disease is discussed.*

ALEXEJEFF-GOLOFF (1929) was the first to report the recovery of *Mycobacterium johnei* from a bovine foetus. Circumstantial evidence of congenital infection was given by Dunkin (1935) who described a clinical case of the disease in a 3-year-old bull whose dam was a clinical case and which had been reared in isolation. Conclusive evidence of infection of the foetus *in utero* was presented by Pearson & McClelland (1955). Lawrence (1956) examined foetuses from 24 infected dams, 19 of which were clinically affected, and found evidence of infection in 5 foetuses. Doyle (1958) also examined foetuses from 24 clinically affected dams and isolated *M. johnei* in 9 cases.

In abattoir surveys in England, the incidence of infection with *M. johnei* in adult cattle has been found to range from 7·5 to 17 per cent. (Rankin, 1954 ; Taylor, 1952 ; Smith, 1954). By comparison, the death rate due to Johne's disease in one part of England has been estimated to be 1 per cent. (Withers, 1955, 1957).

The object of the present survey was to determine the incidence of congenital and neonatal infection in young calves in South-west Scotland where Johne's disease is endemic. It was designed to show whether calves taken at random would be suitable for experimental work, where animals free from *M. johnei* infection are required.

Materials and Methods

The calves used in this survey were bought locally in groups of approximately 40 and slaughtered later the same day. All were healthy bull calves of the local dairy breeds and were considered to be under 1 week of age.

A piece of terminal ileum, the ileo-caecal lymph node and 3 or 4 portions from the chain of mesenteric lymph nodes were taken from each calf and stored in sterile containers at –10° C. until they were cultured. Blocks of tissue from the same areas were fixed in corrosive formol solution for histological examination. The tissues for cultural examination were macerated and pooled; 2 g. of the pooled material were ground in a sterile Griffith's tube with 10 ml. of 0·85 per cent. sterile saline solution. The resulting suspension was transferred to a sterile universal container and an equal volume of 10 per cent. oxalic acid was added. Each universal container was placed in a water bath at 37° C. for 30 minutes, centrifuged at 3,000 r.p.m. for 30 minutes and the deposit sown on 4 slopes of Lowenstein-Jensen medium modified with 1 per cent. w/v heat-killed *M. phlei*. Incubation was at 37·5° C. for 16 weeks. Colonies of acid alcohol-fast bacteria morphologically resembling *M. johnei* were sub-cultured on glycerol agar, Lowenstein-Jensen and *M. phlei* modified Lowenstein-Jensen media. Those which showed visible signs of growth after 8 weeks on the latter medium only were regarded as *M. johnei*.

Results

Cultural examination : Of 158 calves examined *M. johnei* was recovered from 1 only, that is 0·63 per cent.

Histological examination : On detailed histological examination, neither lesions nor organisms were found at any site in any case.

Discussion

Owing to the inaccuracies of the methods used, that is the lethal effects of oxalic acid and the impractibility of examining all the potentially infected sites, the true incidence may be greater than that found in the present series. However it would appear that only a very small proportion of calves of the local dairy breeds are congenitally infected with *M. johnei* or acquire infection within the first few days of life. In the absence of a known *M. johnei*-free source of experimental animals, calves from a source similar to that used in this survey would provide experimental calves with a low incidence of *M. johnei* infection.

Since the infection rate of calves under one week old was 0·63 per cent. and the expected incidence of infection in adults should range from 7·5 to 17 per cent., many animals must become infected

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A Method for Closed-circuit Anaesthesia in the Pig

BY

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SUMMARY.—1. *A method of anaesthesia is described suitable for large pigs.*

2. *After pre-medication with chlorpromazine, anaesthesia is induced with pentobarbitone given intravenously and is maintained with cyclopropane used in a closed circuit.*

3. *The necessary apparatus is described, including a combined trolley and operating table.*

INVESTIGATIONS undertaken at the Institute of Animal Physiology necessitated repeated laparotomies on pigs weighing 100 to 250 kg. and so a safe and easily controllable method of anaesthesia was required. Apart from difficulties of administration, inhalation anaesthesia using chloroform is associated with a grave risk of respiratory failure (Wright, 1952) and when ether is used adequate surgical anaesthesia is difficult to attain without special apparatus. The barbiturates, given intravenously, are moderately satisfactory but they act only for a short period and repeated intravenous injections are often troublesome and inconvenient to give during an operation.

In view of the fact that closed-circuit cyclopropane-oxygen anaesthesia with carbon dioxide absorption has proved successful in the dog, goat, sheep (see Wright, 1957) and horse (Dyce, Jones & Wadsworth, 1952) and is used routinely for general anaesthesia in goats and sheep in this Institute, this method appeared to merit a thorough trial in the pig.

This paper describes a satisfactory routine procedure using cyclopropane, which has been developed in the course of 87 operations on a total of 26 pigs, most of which have undergone three or four laparotomies. The procedure includes preliminary sedation of the animal with chlorpromazine and is facilitated by the use of a combined trolley and operating table which reduces the considerable handling problems associated with large anaesthetised pigs.

Special Apparatus

(*a*) *Combined Operating Table and Trolley*

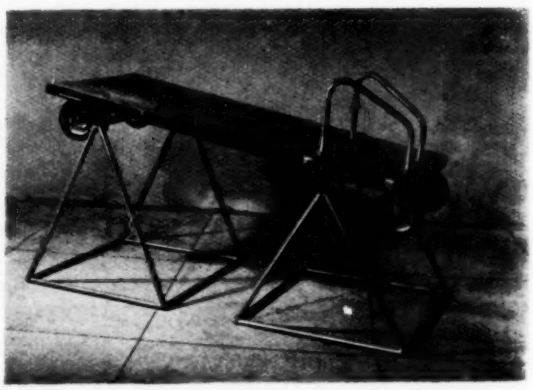

FIG. 1.—Combined operating table and trolley.

The essential features are shown in Fig. 1. The table is made of 18-gauge galvanised steel sheet attached to a rectangular frame of angle-iron strengthened by 2 longitudinal members and 4 corner brackets, the whole being mounted on 4 rubber-tyred castors. Four metal lugs, attached to the frame as shown, rest on trestles and so convert the trolley into an operating table. The trestles are welded from 1-in. steel tube, and one is 6 in. higher than the other so that the table has a 20° slope. The anaesthetised pig is held in position by a detachable steel support which can be

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A Survey of the Incidence of *Mycobacterium johnei* Infection in Calves—*Concluded.*

subsequent to their first few days of life. There are several sources of infection available to calves: (*a*) faeces from infected adults, whether clinical cases or not, (*b*) faeces from congenitally infected calves, from birth onwards (Cunningham & Gilmour, unpublished), (*c*) faeces from calves which become infected. Experimentally it has been shown that resistance to Johne's disease increases with age and that very young calves are most susceptible (Taylor, 1953). It is evident therefore that the practice of keeping calves in communal pens for the first few months of life plays an important part in the epidemiology of the disease.

In infected herds where it is the normal practice to rear calves in communal pens, *i.e.* most dairy herds, it may be possible to control Johne's disease by rearing calves in individual pens for the first few months of life.

Acknowledgment.—The authors wish to acknowledge the interest shown by Dr. W. I. M. McIntyre in this work.

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bolted to the frame, and by ropes looped around the animal's legs and tied to the steel handles which project from the sides of the table.

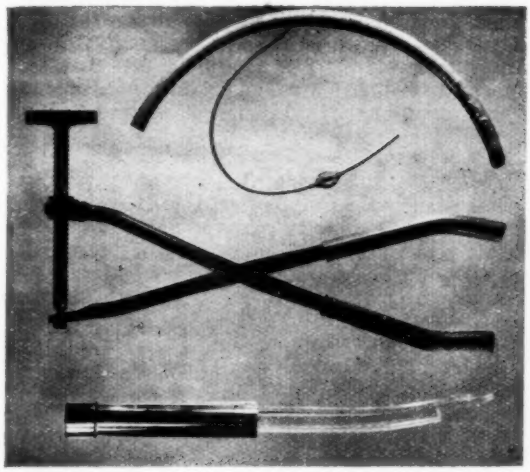

FIG. 2.—Jaw retractor, laryngoscope and Magill endotracheal tube.

(*b*) *Jaw Retractor* (Fig. 2)

This is a scissor-type retractor actuated by a screw with a square-cut thread of coarse pitch. The arms are made from $\frac{3}{8}$-in. steel rod and the tips are rubber shod.

(*c*) *Illuminated Laryngoscope* (Fig. 2)

This is made from $\frac{3}{4}$-in. Perspex rod, slightly curved, and cut to provide a spatulate tip. The metal battery case forms the handle.

(*d*) *Cuffed Endotracheal Tube* (Fig. 2)

It has not been found necessary to use a tube of larger diameter than the Magill No. 10, but it is convenient to have one of more than standard length (British Oxygen Company).

(*e*) *Anaesthetic Apparatus*

A portable anaesthetic apparatus (British Oxygen Company, MS 95, with rebreathing attachment and flowmeter unit) has been used, but the 1-gallon rebreathing bag supplied with the apparatus has been replaced by a 2-gallon bag.

Pre-medication

Food is withheld for 24 hours prior to operation and the animal is weighed during this period to avoid unnecessary excitement immediately before anaesthesia. On the morning of operation chlorpromazine hydrochloride (Largactil, May & Baker) is injected intramuscularly in a dose of 2·02 to 2·5 mg. per kg. bodyweight. The pig then remains undisturbed in its pen for 1 to $1\frac{1}{2}$ hours, which allows time for the sedative effect of chlorpromazine to develop. The degree of sedation produced by this dose of chlorpromazine has varied considerably. In some animals there was a marked drowsiness and lethargy whilst in others there was no apparent change in behaviour. This individual variation has also been noted in the pig by Ritchie (1957) and in the horse by Graham (1956) who suggests that it may be due to the dissimilarities in temperament of different animals. To achieve adequate sedation therefore it may be necessary to exceed the stated doses for individual pigs. Nevertheless, in practically all the animals which received 2·0 to 2·5 mg. per kg. chlorpromazine, whether they showed obvious sedation or not, subsequent intravenous injection was facilitated and the anaesthetic properties of the induction agent, pentobarbitone, appeared to be potentiated.

Induction

After washing and shaving the ear, anaesthesia is induced with an injection of sodium pentobarbitone solution into one of the veins on the back of the ear. This can be done in the animal's pen and the injection may be given with or without restraint, depending on the degree of sedation brought about by the chlorpromazine. When restraint is necessary, a rope noose around the upper jaw with the free end attached to a ring in the wall is satisfactory.

As the veins on the dorsum of the ear provide the most convenient route for intravenous injection in the pig it is important to conserve them as far as possible if repeated operations are to be performed upon the same animal. Two practical points which appear to help are the use of a fine-bore needle (No. 16) and of an aqueous solution of pentobarbitone. The dosage has ranged from 10 to 20 mg. per kg. bodyweight, the required quantity of the powder (Abbotts Nembutal Powder) being dissolved in 8 to 10 ml. of sterile normal saline a short time before use. The injection is given fairly rapidly, the aim being to produce moderately deep anaesthesia of short duration to facilitate the endotracheal intubation. Atropine sulphate (0·2 mg. per kg.) is injected subcutaneously to reduce the secretion of saliva and mucus which may be troublesome during the subsequent intubation.

Intubation

The animal is placed on its left side on the trolley, and wheeled to the operating room where the endo-

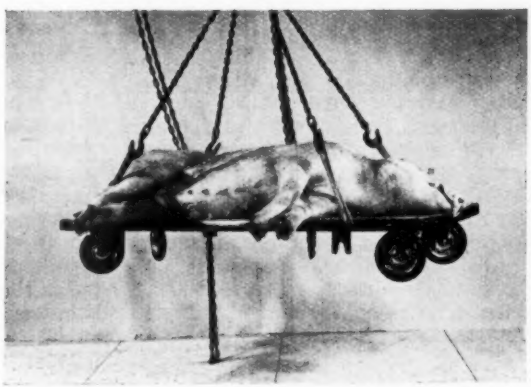

FIG. 3.—Sow in position for intubation.

FIG. 4.—Jaw retractor in use, and endotracheal tube inserted.

FIG. 5.—Interior of mouth, showing apex of epiglottis when the tongue is depressed by the laryngoscope.

tracheal tube is inserted. This is made easier if the trolley can be raised as shown in Fig. 3 and held level at a height convenient to the operator. If the head is slightly extended the airway will be nearly straight. The mouth is opened by means of the retractors, which are placed so that pressure is applied to the hard palate and to the floor of the mouth, just behind the incisors (Fig. 4). The laryngoscope is introduced into the mouth over the dorsum of the tongue, and the root of the tongue is depressed by means of the spatulate end (Fig. 5). The apex of the epiglottis may now be visible although more frequently it lies on the pharyngeal side of the soft palate and cannot be seen at this stage. It is, however, a simple matter to raise the soft palate with the laryngoscope and so bring the epiglottis into view. The tip of the laryngoscope is then used to hold the apex of the epiglottis against the root of the tongue and so bring the interior of the larynx into view. The tip of the endotracheal tube is gently inserted between the vocal cords and pushed down into the trachea (Fig. 6). A metal rod in the tube serves to hold it straight until its tip is inserted into the larynx. The rod is withdrawn as the tube is passed into the trachea. The cuff is inflated and the retractor is then replaced by a small wooden gag. The tube is passed through a hole in this gag and is connected to the anaesthetic apparatus (Fig. 7). Before the connexion is made the trolley is lowered on to the trestles and the animal is secured in the appropriate operating position. The slope of the table, primarily designed to hold the animal in a supine position with the shoulders lower than the pelvis, makes it possible to arrange the anaesthetic apparatus so that mucus, and fluid formed by condensation within the gas line, flow downwards towards the rebreathing bag.

Maintenance Anaesthesia

Immediately the endotracheal tube is connected to the anaesthetic apparatus, oxygen and cyclopropane in the proportions of 2 or 3 to 1 are run into the circuit until the rebreathing bag is moderately full. For pigs weighing 100 to 150 kg. the gas flows are then adjusted to 250 to 350 c.c. oxygen and 50 to 100 c.c. cyclopropane, per minute. Heavier pigs consume more oxygen; they also require appreciably more cyclopropane per kg. bodyweight to maintain surgical anaesthesia. This is apparent from Fig. 8 where the cyclopropane consumption per unit weight in 21 operations of similar duration is plotted against the bodyweight of the animal. Cyclopropane is readily soluble in body-fat and the increased cyclo-

FIG. 6.—Dissection of head of sow with R. ramus removed to show route of intubation.

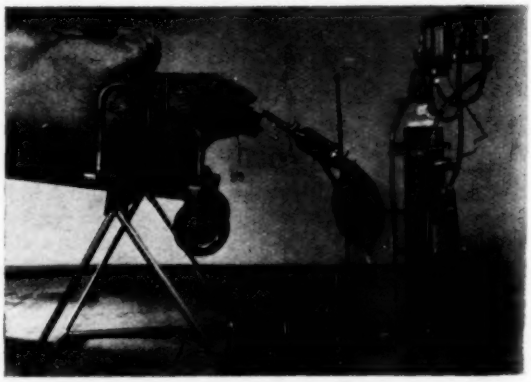

FIG. 7.—Animal in operating position, and connected to the anaesthetic apparatus.

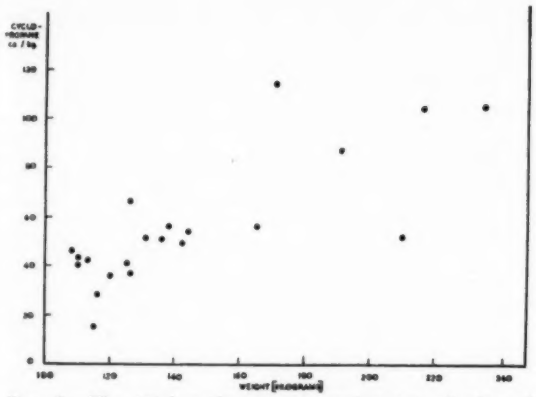

FIG. 8.—The total cyclopropane requirement of pigs of varying bodyweight during operations of similar duration (1½ to 2 hours).

propane requirement may be related to the greater body-fat content of large animals.

The whole process between induction and connexion to the anaesthetic apparatus should be done as expeditiously as possible. This ensures that anaesthesia proceeds smoothly as the effect of the pentobarbitone wanes. During the first 15 to 30 minutes of cyclopropane administration the depth of anaesthesia is assessed at frequent intervals. The corneal reflex, and the response when the skin is pricked with a needle, are useful guides at this stage. The aim is to maintain the animal at a medium depth of anaesthesia, *i.e.*, with a sluggish corneal reflex and loss of the response to skin pricking. This is done by increasing the flow of cyclopropane, and when a suitable depth of anaesthesia has been established it can usually be maintained by occasional adjustment of the cyclopropane flow. An example is given in Table I which shows how the flow of oxygen and cyclopropane, and the percentage of cyclopropane present in the gas mixture at any one time, varied during an actual operation. In the particular anaesthetic apparatus used here the soda-lime container cannot be cut out of the circuit, and hence CO_2 absorption goes on continuously. The soda-lime container holds about 400 gm., sufficient for an operation lasting about 2 hours.

TABLE I

PROGRESS OF A TYPICAL OPERATION
ANIMAL—LARGE WHITE SOW

Date : 14.8.56		Number : BL 19		Weight : 126.4 kg.	
Pre-medication :	Chlorpromazine, 250 mg., i.m.				9.30 a.m.
Induction :	Pentobarbitone 30 grains (2 g.), i.v.				10.36 a.m.
Atropine :	25 mg.				10.38 a.m.
Connection to anaesthetic apparatus				... ...	10.48 a.m.
Progress :					
Time, a.m.	Oxygen c.c. per min.	Cyclo-propane c.c. per min.	Mixture per cent. C_3H_6	Respira-tions per min.	Reflexes
10.50	350	50	14·2	—	Corneal + +
10.51	350	100	28·5	—	Skin twitching +
10.52	350	100	28·5	9	Corneal +
10.57	—	—	—	8	
11.01	350	50	14·2	—	Quiet
11.05	350	100	28·5	—	Skin twitching +
11.10	300	100	33·3	—	Quiet
11.11	300	100	33·3	7	,,
11.21	Incision				
11.22	300	50	16·6		
11.30	300	100	33·3	—	Skin twitching +
11.40	300	100	33·3	7	Quiet
11.55	300	100	33·3	7	,,
12.11	300	100	33·3	6	,,
12.20	Operation finished				

Recovery

Immediately the operation has been completed the endotracheal tube is removed. Recovery is rapid, vigorous reflexes being present after 1 to 2 minutes and movements of the head and limbs occurring after about 5 minutes. The majority of pigs stand within 2 hours of operation and will usually take food shortly afterwards. Pigs which have been operated upon are kept in a recovery pen for 2 to 3 days.

Complications

Cessation of respiration after giving pentobarbitone has occurred on a number of occasions. This is a common complication in large pigs but it is usually easy to overcome by applying artificial respiration (Wright, 1957) which is facilitated by tracheal intubation and the use of a closed circuit. There have been 2 deaths during anaesthesia in the course of 87 laparotomies undertaken on adult pigs. Both animals were large sows; in one case breathing stopped after intubation but before cyclopropane was administered, and in the other cyclopropane administration had begun but surgical anaesthesia had not been achieved. Artificial respiration was ineffective in both cases.

Acknowledgments.—We are grateful to Dr. L. W. Hall, Department of Veterinary Clinical Studies, Cambridge, for his constructive criticism of the manuscript ; to Mr. P. N. O'Donoghue and Miss P. Bradley for technical assistance ; to the late Mr. A. W. Attwood for the photographs and to Mr. F. J. Seeley for construction of the operating table and jaw retractors.

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TWIN-CALF EXPERIMENTS

Ministry support has been given to a plan to conduct twin-calf experiments in East Anglia. An application for a grant of £500 from the Ministry to run the tests has been successful and work on the project is expected to start at once. The experiments, which will be carried out by Cambridge A.I. Centre, will involve about 100 dairy cows and a few beef cattle.

Apart from the actual experiments on finding out whether twin-calf production is possible on a commercial basis the Centre is also interested in combating the undesirable effects of twinning on calves.

The Use of Living Attenuated Vaccines in the Control of Fowl Typhoid

BY

R. F. GORDON, J. S. GARSIDE and J. F. TUCKER

Houghton Poultry Research Station

SUMMARY.—(1) Evidence is submitted confirming the efficiency of attenuated live vaccines of Salmonella gallinarum, *9S and 9R in conferring immunity against fowl typhoid.*

(2) There was no difference in susceptibility to, nor in response to, either vaccine amongst the four breeds tested.

(3) Vaccination at 8 weeks of age produces an appreciably better immunity than at 4 weeks of age.

(4) The use of vaccine 9R in the field appears justified in that it confers an appreciable degree of immunity without seriously interfering with the routine blood test for carriers of Salm. pullorum *and, in addition to possessing a low level of virulence for chicks, its transmission through the egg from vaccinated laying birds appears to be almost negligible.*

Introduction

BOTH Williams Smith (1956a) and Wilson (1956) in reviewing the literature on fowl typhoid vaccine state that the bulk of available evidence indicates that dead vaccines prepared from cultures of *Salmonella gallinarum* are of little value in the control of this disease. Wilson (*loc. cit.*) reported on an attenuated live vaccine which although it produced a strong immunity was of little practical value since it was still sufficiently virulent to cause a mortality of 37 per cent. in the vaccinated birds. Williams Smith (*loc. cit.*) however showed that a good immunity could be produced in chickens against oral infections with *Salm. gallinarum* by the use of either of two live attenuated vaccines, one smooth (9S) and one rough (9R). Chickens vaccinated with 9S were completely immune when challenged 34 weeks later, while the immunity to 9R waned after 12 weeks. Unfortunately vaccine 9S produced agglutinins to the rapid whole-blood pullorum agglutination test, a disadvantage when considering the use of this vaccine in relation to the Poultry Stock Improvement Plan ; furthermore this vaccine was lethal for day-old chicks although its virulence was not increased by passage, whilst its use in laying hens was accompanied by a marked reduction in egg production. In contrast vaccine 9R did not produce demonstrable agglutinins in chickens, was not lethal for day-old chicks, and did not seriously interfere with production in laying hens. Some transmission of the vaccinal strains was encountered and of 190 eggs laid by fowls vaccinated with 9R, 9 (4·7 per cent.) yielded the vaccinal strain, whilst 5 (4·6 per cent.) of 108 eggs laid by the Group vaccinated with 9S yielded 9S.

Harbourne (1957) carried out field trials with both vaccines, 9R and 9S, and reported that they were equally effective in reducing the mortality from fowl typhoid. Where the vaccines were used in flocks free from the disease there was no apparent interference with egg production.

Williams Smith (1956b) reported a marked difference in resistance to experimental infection to fowl typhoid in four breeds maintained at the Houghton Poultry Research Station varying from a percentage mortality rate of 93 in R.I.R., 82 in Barred Rocks, 90 in Brown Leghorns, and 11 in White Leghorns ; whilst similar tests with chickens originating from a commercial hatchery also showed strain variations, the mortality rate after infection ranging from 16 per cent. in Black Leghorns to 36 per cent. in White Leghorns and Brown Leghorns, and 80 to 91 per cent. in Light Sussex.

Present Investigations

In view of the promising results obtained with these vaccines in both experimental and field outbreaks, the investigations now reported were designed to clarify the following points :—

1. Breed variation to vaccination with 9R and 9S, and the efficiency of these vaccines in controlling experimental *Salm. gallinarum* infection in chickens at 4 weeks old and 8 weeks old.
2. The effect of the use of these vaccines on the routine blood test for pullorum disease.
3. The extent of the transmission of vaccinal and challenge strains in fresh eggs, dead embryos, and chicks hatched from eggs produced by vaccinated birds before and after challenge.

Materials and Methods

All chicks and fowls came from the 4 closed flocks kept on the Station : White Leghorns, Brown Leghorns, Barred Rocks, and Rhode Island Reds or their crosses. Housing and feeding were to standard practice : chicks were housed on slatted floor fold units raised off the ground and fed on the normal grower's rations used on the station to the formula described by Chubb, Gordon and Tucker (1958). Vaccines 9R and 9S were prepared by the method of Williams Smith (*loc. cit.*) but standardised to contain 50,000,000 viable organisms per ml., 1 ml. inoculated subcutaneously constituting the vaccine. The administration of the challenge strain of *Salm. gallinarum*, and the examination of eggs and contents were by the methods described by Williams Smith (1956a) and the bacteriological examination of carcases by the technique of Gordon and Tucker (1957).

Agglutination tests consisted of the rapid whole blood test together with the slow tube test using the drop technique, complete agglutination at 1 : 20 being considered indicative of infection. The acriflavine

test of Braun and Bonestell (1947) was used to test cultures for roughness when necessary.

Experimental Results

Breed Variations and Efficiency of Vaccination

A total of 651 pure-bred chickens from the 4 breeds were tested at different times in 9 batches, 4 batches of 4-week-old chickens, and 5 batches of 8-week-old chickens. The 9 batches were divided on each occasion into 3 groups, one group consisting of 9R vaccinated chickens plus unvaccinated in-contact chickens, a second group of 9S vaccinated chickens plus unvaccinated in-contact chickens, and a third of unvaccinated chickens reared in isolation from the previous groups. The unvaccinated in-contact chickens were included to ascertain if transmission of the vaccinal strains occurred to any extent from vaccinated to unvaccinated birds by cohabitation. All chickens in each batch, vaccinated, unvaccinated and isolated controls were challenged with a virulent culture of *Salm. gallinarum* 4 weeks after the vaccinated chicks received their vaccine, and the results observed for a period of 21 days. Tables I and II show the results.

The combined results of column 5 in Tables I and II show that the mortality rate in all the chickens challenged after vaccination with Strain 9S averaged 2·1 per cent. as against 6·7 per cent. in those challenged after vaccination with Strain 9R. These figures compared with an average mortality rate of 65·2 per cent. for all the control groups confirm the efficiency of both vaccines in conferring protection against infection with *Salm. gallinarum*, the smooth strain being slightly the more effective of the two. The 8-week-old chickens responded to both vaccines better than the younger ones, vaccine 9S giving 100 per cent. protection, and vaccine 9R only slightly less ; but even in

TABLE I
BREED RESPONSE TO VACCINATION WITH VACCINES 9R AND 9S FOLLOWED BY CHALLENGE WITH *Salm. gallinarum* OF 4-WEEK-OLD CHICKENS

Vaccine	Vaccinated chickens				Non-vaccinated chickens				
					Controls in-contact			Controls not in-contact	
	Breed	Number vaccinated	Mortality after vaccination, per cent.	Mortality after challenge, per cent.	Number	Mortality before challenge per cent.	Mortality after challenge, per cent.	Number challenged	Mortality after challenge, per cent.
9R	Barred Rock ...	25	0	12·0	10	0	70·0	10	80
	Brown Leghorn...	28	7·0	7·7	10	0	100·0	10	100
	White „ ...	31	3·2	13·3	10	0	50·0	10	30
	Rhode Island Red	33	0	15·1	10	0	50·0	10	50
	Total ...	117	2·5	12·0	40	0	67·5	40	65
9S	Barred Rock ...	26	3·8	0	10	10·0	77·0		
	Brown Leghorn...	27	3·7	7·7	10	10·0	100·0		
	White „ ...	31	0	0	10	0	10·0		
	Rhode Island Red	34	2·9	9·0	10	10·0	77·7		
	Total ...	118	2·6	4·2	40	7·5	66·2		

TABLE II
BREED RESPONSE TO VACCINATION WITH VACCINES 9R AND 9S FOLLOWED BY CHALLENGE WITH *Salm. gallinarum* OF 8-WEEK-OLD CHICKENS

Vaccine	Vaccinated chickens				Non-vaccinated chickens				
					Controls in-contact			Controls not in-contact	
	Breed	Number vaccinated	Mortality after vaccination, per cent.	Mortality after challenge, per cent.	Number	Mortality before challenge per cent.	Mortality after challenge, per cent.	Number challenged	Mortality after challenge, per cent.
9R	Barred Rock ...	18	5·5	0	9	11·0	50·0	8	25·0
	Brown Leghorn...	34	0	5·8	10	20·0	100·0	8	87·5
	White „ ...	20	0	0	10	0	20·0	12	58·3
	Rhode Island Red	19	0	0	10	0	80·0	9	88·0
	Total ...	91	1·3	1·4	39	7·7	62·5	37	64·7
9S	Barred Rock ...	18	5·5	0	9	0	22·0		
	Brown Leghorn...	34	0	0	9	11·0	100·0		
	White „ ...	20	0	0	10	0	10·0		
	Rhode Island Red	19	5·2	0	10	0	90·0		
	Total ...	91	2·7	0	38	2·7	55·5		

the younger chicks a considerable degree of protection was afforded. Neither vaccine appeared to be potentially harmful in use, the losses after vaccination being negligible in both age groups, and further, there was no appreciable spread to the in-contact unvaccinated chickens. It is not possible to say definitely that the mortality before challenge in any of the groups was due to the vaccinal organism although *Salm. gallinarum* was isolated from the tissues and/or intestines of 13 out of the 16 chickens which died at this stage, but there was no evidence clinically, or on autopsy, that fowl typhoid was the primary cause of death. In each instance the culture isolated corresponded in dissociation with the vaccinal strain. There was no constant variation in the susceptibility of the different breeds to either vaccine, and little variation in their immune response as judged by mortality figures after challenge.

It is also noticeable that in all the unvaccinated groups the White Leghorn chickens were distinctly less susceptible to *Salm. gallinarum* infection than were the chickens of the other breeds, a feature also recorded by Williams Smith (1956b).

Effects of Vaccination on the Use of the Routine Whole-blood Test for Pullorum Disease

The 651 chicks referred to in the previous experiment were all tested by means of the rapid whole-blood test, and the tube test for pullorum disease 4 weeks after vaccination (and immediately before challenge), and again 3 weeks after challenge, with the results shown in Table III.

TABLE III
EFFECTS ON THE ROUTINE WHOLE BLOOD TEST FOR PULLORUM DISEASE FOLLOWING THE USE OF VACCINES 9R AND 9S

Group	Before challenge		After challenge	
	Number of birds tested	Number of birds giving a positive reaction	Number of birds tested	Number of birds giving a positive reaction
9R vaccine ...	208	5 (2·4%)	188	154
9S " ...	209	198 (94·7%)	199	196
In-contact to 9R	79	0	27	22
" 9S	78	1 (1·2%)	30	24
Controls ...	77	0	27	26

These results confirm that vaccination with the rough strain 9R is not likely to interfere to any extent with the routine use of the blood test for pullorum disease, less than 3 per cent. of 9R vaccinated chicks and none of the unvaccinated chicks reared in-contact with them reacted to either the whole-blood test or the serum tube test. Vaccine 9S as expected did produce reactors, and showed 94·7 per cent. reactors in the vaccinated chicks, and 1·2 per cent. of the chicks reared in-contact with them, some of the titres of these reacting birds reaching as high as 1 : 1,600. At the same time it is obvious that if vaccinated birds do come into contact with infection and are transformed into " carriers " of the field strain, the routine blood test will reveal these " carriers."

The Transmission of Vaccine Strains and/or Challenge Strains in Fresh Eggs, Incubated Eggs, Dead Embryos and Chicks Hatched from Eggs Produced by Vaccinated Birds

In this experiment 98 W.L. × R.I.R. pullets and 7 Brown Leghorn cockerels, all negative to the tube test for pullorum disease were divided into 6 groups. Groups 1 to 4 and Group 6 consisted of 14 pullets and 1 cockerel whilst Group 5 consisted of 28 pullets and 2 cockerels.

Groups 1 and 3 were vaccinated with vaccine 9R. Groups 2 and 4 with vaccine 9S and Groups 5 and 6 left unvaccinated. Twenty-eight days after this vaccination Groups 3, 4 and 5 were challenged each with a similar graded dose of a virulent strain of *Salm. gallinarum* (S.G.9), the remaining groups being left unchallenged. Groups were housed separately and received ordinary layer's rations.

During the period between vaccination and challenge, eggs from all groups were collected daily and examined bacteriologically for the presence of the vaccinal organism. All eggs laid by birds in Groups 1 to 4 were examined, but only random collections made from Groups 5 and 6. After the challenge of Groups 3, 4 and 5 the collection and examination of eggs from all groups continued in the same way for a period of 3 weeks, but after this time and for the ensuing 10 weeks a proportion of eggs collected were set aside daily and incubated in batches at weekly intervals until a total of 200 eggs had been incubated from each group. Eggs not saved and incubated were examined daily as before. This procedure was continued until the end of the experiment 32 weeks after the original vaccination.

In all, 688 eggs were examined from Group 1 ; 273 from Group 2 ; 957 from Group 3 ; 537 from Group 4 ; 518 from Group 5 ; and 103 from Group 6 (excluding the 200 eggs from each group set aside for incubation). The variation in numbers (apart from Group 6) is accounted for by an outbreak of egg eating which caused the loss of a large number of eggs, particularly from Group 2. Furthermore, following the administration of the challenge dose, and within 3 weeks 19 birds, including the 2 cockerels, died in Group 5, so that to allow this group to continue to take part in the test another Brown Leghorn cockerel was placed in the pen. This bird was unchallenged and survived infection. No deaths occurred within the other challenged groups during this period.

The eggs for hatching were incubated in a natural draught incubator and all dead embryos and infertile eggs removed by candling on the 14th day. These, together with dead-in-shell chicks and the shells of all eggs which subsequently hatched were subjected to bacteriological examination. Hatched chicks were reared in their separate batches on wire-floored brooders for a period of 3 weeks during which time all chicks which died were examined bacteriologically. The results of these tests are tabulated in Tables IV and V. (See page 303).

The Isolation of Salm. gallinarum *from Fresh Eggs*

The results recorded in Table IV showed that there was some, but not frequent, transference of the vaccinal strains to eggs laid by vaccinated birds.

TABLE IV
ISOLATION OF *Salm. gallinarum* FROM FRESH EGGS OVER A PERIOD OF 32 WEEKS

Group	Vaccine	28 days before challenge		Challenge strain	196 days after challenge		Dissociation	Period after vaccination of last infected egg
		Number of eggs cultured	*Salm. gallinarum* isolated		Number of eggs cultured	*Salm. gallinarum* isolated		
1	9R	688*	13 (1·9%)	Not challenged	—	—	All rough	31st week
2	9S	273*	5 (1·8%)	Not challenged	—	—	All smooth	29th „
3	9R	105	2 (1·9%)	S.G.9	852	31 (3·6%)	Before challenge 2 cultures R. After „ 13 „ R. 18 „ S.	29th „
4	9S	64	1 (1·5%)	S.G.9	473	14 (3·0%)	All smooth	29th „
5	None	30	0	S.G.9	488	28 (5·8%)	„	25th „ (21 weeks after challenge)
6	None	103*	0	Not challenged	—	—	—	—

* Totals for the full period of 32 weeks.

TABLE V
ISOLATION OF *Salm. gallinarum* FROM INFERTILE EGGS, DEAD-IN-SHELL, DEAD EMBRYOS, AND CHICKS HATCHED FROM VACCINATED AND/OR CHALLENGED BIRDS

Group	Origin of eggs: Vaccinated or unvaccinated	Challenged with	Number of eggs incubated	Number of infertile and dead-in-shell	*Salm. gallinarum* isolated from —	Number of chicks hatched	*Salm. gallinarum* isolated from shells	Number of chicks dying during first 3 weeks	*Salm. gallinarum* isolated from chicks	Total isolations of *Salm. gallinarum* and dissociation of strains
1	Vaccinated with 9R	None	200	152	0	48	0	10	1	1 (rough)
2	„ „ 9S	None	200	174	27	26	0	0	0	27 (all smooth)
3	„ „ 9R	S.G.9	200	127	27	73	15	9	3	45 (21 rough, 24 smooth)
4	„ „ 9S	S.G.9	200	154	58	46	12	24	16	86 (all smooth)
5	Unvaccinated ...	S.G.9	200	113	69	87	22	38	25	91 („)
6	„ ...	None	200	131	0	69	0	14	0	0

Using vaccine 9R the rough strain was isolated during the period of the experiment from approximately 2 per cent. of eggs laid by the birds in Group 1. This frequency was repeated in Group 3 before challenge but after challenge the smooth challenge strain made its appearance, in addition to the rough strain, and with slightly greater frequency, raising the total number of infected eggs to 3·6 per cent. Very similar figures were recorded for the isolation of strain 9S in Group 2, and also in Group 4 before challenge, whilst after challenge the figure in the latter group rose to 3 per cent. Presumably here also, the strains isolated comprised both vaccinal and challenge organisms although no distinction could be made on examination. In both Groups 3 and 4, the total isolations was approximately half of that recorded for the unvaccinated, challenged controls. Infected eggs appeared at irregular intervals in all vaccinated and/or challenged groups, and persisted until the 31st week in the case of Group 1, and the 29th week in Groups 2, 3 and 4.

The Isolation of Salm. gallinarum *from Infertile Eggs, Dead-in-shell, and Shells, and Chicks*

Owing to local electricity failures during the course of the experiments which interfered with the incubation and subsequent rearing of the chicks it is difficult to interpret the findings recorded on Table V which illustrate the recovery of the vaccinal strains from eggs laid by vaccinated birds.

In Group 1 from eggs from birds vaccinated with strain 9R the vaccinal strain was recovered on only one occasion, from a hatched chick, and from no other source, infertile eggs, dead embryos or shells of hatched chicks. Conversely, the vaccinal strain 9S was isolated on 27 occasions from infertile eggs and dead embryos originating from the birds vaccinated with 9S, but not from any of the chicks. The difference between the behaviour of the 2 strains is most marked. Furthermore, the level of isolations in Group 2 is much higher than that recorded for fresh eggs from the same group, a feature which might be explained by assuming the growth of organisms in the egg during the period of storage and incubation, thereby allowing minimal infections to become apparent ; though why the same mechanism has not operated in Group 1 is difficult to explain. In the 2 breeding pens vaccinated respectively with 9R and 9S, and subsequently challenged with the virulent culture S.G.9 (Groups 3 and 4), *Salm. gallinarum* was isolated on 27 occasions from infertile eggs and dead embryos, and on 15* occasions from eggshells and

* This represents the total number of infected eggs, some of them being positive on both shells and in chicks.

chicks hatched from the 9R group ; whereas in the pen vaccinated with 9S the recovery rate was 58 from infertile eggs and dead embryos, and 16 from eggshells and hatched chicks. Group 5, the unvaccinated, challenged group, gave figures of 69 and 37 respectively. In all instances the level of isolations was considerably higher than would be anticipated as a result of the examination of fresh eggs. The single strain isolated in Group 1 proved on examination to be the rough strain whilst in Group 3 where again vaccine 9R had been employed, rough and smooth strains were isolated in roughly similar proportions to those recorded from fresh eggs, although now in greater numbers.

Surviving chicks of all groups were challenged when 21 days of age with a virulent culture of *Salm. gallinarum* and the resultant mortality of all groups was similar at between 60 and 70 per cent., no protection being evinced in the progeny of pullets vaccinated with either vaccine compared with the progeny of unvaccinated controls.

The Virulence of 9R and 9S Cultures for 1-day-old Chicks

Williams Smith (1956a) reported that intramuscular injections of 0·1 ml. of a 24-hour broth culture of strain 9S was lethal to day-old chicks, but a similar dose of strain 9R was not. In order to check the pathogenicity of the cultures used in this investigation batches of chicks were infected either orally or subcutaneously with the 2 cultures and compared with control chicks receiving virulent *Salm. gallinarum*. All inocula consisted of 18-hour-old broth cultures of each strain standardised to 50,000,000 organisms per ml. and administered subcutaneously or *per os* in doses of 0·2 ml. Chicks were observed for 21 days after which all survivors were killed and examined bacteriologically. The numbers of chicks challenged together with the results are set out in Table VI.

TABLE VI
VIRULENCE OF 9R AND 9S VACCINES TOWARDS DAY-OLD CHICKS

Culture and route of inoculation	Number of chicks	Number of deaths	Number of positive cultures from survivors at 21 days
9R, 0·2 ml. orally	25	6	12 (all rough)
9S, 0·2 „	24	24	—
S.G.9, 0·2 „	25	24	0
9R, 0·2 ml. subcutaneously	20	1	10 (all rough)
9S, 0·2 „	20	16	3
S.G.9, 0·2 „	20	18	1

The results showed that vaccine 9S was as harmful to day-old chicks as was the normal virulent strain of *Salm. gallinarum*. At the same time vaccine 9R was less virulent but not completely so in that in these tests 24 per cent. of treated chicks died after the oral administration of the culture, and 5 per cent. after subcutaneous inoculation in spite of the fact that the dose of organisms was one-fifth of that used by Williams Smith for intramuscular inoculation in his series of experiments.

Discussion

The results have confirmed the observations of Williams Smith that attenuated live cultures of *Salm. gallinarum* are highly effective in promoting immunity against infection with this organism, and furthermore are equally effective in a dose of one-tenth the strength. reported by him. The avirulent smooth strain 9S provided the better immunity but has the disadvantage of interfering with the blood test used to detect carriers of pullorum disease, and therefore would present difficulties if used in flocks participating in the Poultry Stock Improvement Plan. The rough variant 9R however, appears only slightly less effective, and would not interfere markedly with the blood test so that its use is fully justified. Administration of the vaccine would seem to be more effective in birds over 8 weeks old, so that for practical purposes vaccination should be practised any time after the birds have reached this age, and preferably before 16 weeks of age (*i.e.*, before egg production starts).

There was no evidence of marked variation in the immune response, or susceptibility to either of the vaccines, amongst the 4 breeds tested.

Transmission of both strains, 9R and 9S occurred through the egg and apparently this could continue over long periods since 9R was recovered from 1 egg laid 31 weeks after vaccination and 9S 29 weeks after vaccination. How long this might have continued is not known since the experiment was terminated after 32 weeks. It is, however, a measure of the persistence of the vaccinal organisms in the tissues of some of the vaccinated birds, and contrary to Williams Smith's (1956a) observation in which the organisms were not recovered after 3 weeks in the case of 9R vaccination, and 10 days following 9S vaccination. All 14 strains of *Salm. gallinarum* recovered from eggs, and the 1 chick from the 9R vaccinated birds during these 32 weeks were found, on examination, to be rough, and to correspond to the vaccinal strain, indicating the stability of the strain which seemed to have no tendency to revert.

The recovery rate of vaccinal strains from fresh eggs was low but increased on storage and incubation. The risk of egg transmission seems to be slight as far as vaccine 9R is concerned since the recovery of the strain from 200 eggs was from 1 hatched chick alone ; no successful isolations being made from infertile eggs, dead embryos or shells of hatched eggs. The level of recoveries of the organisms from fresh eggs in these experiments was lower than the figures quoted by Williams Smith in his observations.

Both vaccines were found to be pathogenic for young chicks when administered *per os*, but less so on subcutaneous injection. Vaccine 9R was much less virulent than 9S, but a 25 per cent. mortality was recorded when it was administered orally, and 5 per cent. when given subcutaneously. These results might be held to mitigate against the use of the vaccine, but since it would not normally be used to any extent in day-old chicks, being far more efficient after the age of 8 weeks, the admitted susceptibility of young chicks need not be taken into account except in so far as the organism might be passed through the eggs of a

(*Concluded at foot of adjoining column*)

Current Literature

BOOK REVIEWS

Ecological Processes. By ALAN MOZLEY. H. K. Lewis & Co., London, 1959. 9s.

Even an energetic field naturalist like Dr. Mozley finds time for meditation. As he walks by his wild lone through the wet, wild woods, or sits on the banks of the great, grey-green, greasy Limpopo River, all set about with fever trees, his thoughts inevitably turn on the mysteries of life and a philosophy of nature must mature in his mind. In yet another of his little books Dr. Mozley serves up the *Weltanschauung* that he has distilled from all his communing with nature. The result is a *chef-d'oeuvre* in many respects to be ranked with that of Professor Teufelsdroeckh.

It is a book which must be read more than once if its burden is not to be overlooked, for it is heavily overlaid with commonplace material some of which is to be found in standard ecological texts. When discovered, the message is not one with which everyone would agree. It appears that snails which are the intermediate hosts of pathogenic trematodes are as unnatural as disease itself and scarcely have a rightful place in the economy of nature. Sordid outcasts, denizens of the fluctuating no-man's-land between communities, they occur in appreciable numbers only in the immature stages of ecological successions. To this extent their abundance and the diseases with which they are associated are most frequently to be seen as just another expression and consequence of human guilt.

It is with his ideas on what he calls " replacement control " that Dr. Mozley reaches his most heterodox. That *Lymnaea truncatula* for example could be replaced by *L. pereger* without an alteration in the physical condition of the habitat seems astonishing. The optimum habitat for one species is not the optimum for the other and if *L. truncatula* predominates in a given site the reason is not merely that it happened to get a toe in first.

Perhaps it is wrong to cavil at details. Here after all is Dr. Mozley's testament. Is it too much to hope that it will be his last?

Meat. A Review of Production, Trade, Consumption and Prices Relating to Beef, Live Cattle, Mutton and Lamb, Live Sheep, Bacon and Hams, Pork, Live Pigs, Canned Meat, Offals and Poultry. Compiled by the Intelligence Branch of the Commonwealth Economic Committee. Published by H.M. Stationery Office. Pp. 112. Price 5s.

This publication contains a wealth of information, largely of a statistical character, concerning exports and imports of live food animals and meat. Marketing, slaughtering information, and world prices are also given. The review covers the years 1953–7, with those for 1938 by way of comparison.

The information so compiled will be of primary interest to those engaged in the wholesale meat trade and to the economist although those of our readers who are intimately concerned with meat production may find it a valuable source of reference.

Lehrbuch der Rinderbesamung (Text-book of Insemination of Cattle). By KARL EIBL. Pp. 502. 201 Figs. 32 Tables. Paul Parey, Berlin, 1959. DM. 74.

The author of this comprehensive text-book on artificial insemination of cattle is a senior State veterinarian, with agricultural qualifications, who is chairman of the West German veterinary A.I. group and has worked in this field for many years as director of one of the most important German A.I. centres, that at Neustadt/Aisch. The book is beautifully produced and richly illustrated. The first section deals exhaustively with the sex organs of the bull, and the characters and evaluation of semen and its dilution and preservation. There are numerous illustrations showing spermatogenesis and spermatozoa with various abnormalities. This section occupies 124 pages. There follows a section of about half that length devoted to the female sex organs, the process of insemination and the resulting conception rate. The third section deals with the place of A.I. in cattle breeding, the choice of bulls, progeny testing, and the methods by which A.I. within a country and traffic in semen from one country to another should be controlled. Two sections are then given over to the organisation of A.I. centres and day-to-day work with the bulls, and with laboratory techniques. The last part of the book describes the process of insemination on the farm. Finally, 2 short appendices give details of the preparation, cleansing, and sterilisation of A.I. apparatus and rules for the effective running of an A.I. centre; the latter include the suggestion that blood grouping should be introduced for all bulls at A.I. centres as soon as possible and not used merely to identify offspring of doubtful parentage.

There are already 2 useful German text-books on this subject, those by Götze (1949) and by Küst and Schaetz (1954), but the volume under review takes account of more recent advances and especially the

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The Use of Living Attenuated Vaccines in the Control of Fowl Typhoid—*Concluded.*

vaccinated breeding flock. The experiments have shown, however, that less than 2 per cent. of eggs laid by 9R vaccinated birds carry the organism and this was not increased on incubation so that the danger of infecting chicks hatched from these eggs is slight, and the disadvantage of possible losses amongst the chicks negligible compared with the obvious advantage of protecting the adults against infection.

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rapid strides made in Germany during recent years. A list of text-books on relevant subjects is given. There are many references in the text to published work of others, but unfortunately they are incomplete, *e.g.* "Irwin (1947)," which makes it very laborious to trace their precise origin. If references are given at all they should be in full.

All who are concerned with A.I. in cattle could profit from consulting this book, and it would seem that an English translation would be well worth while, since although some of the technique and organisation is peculiar to the country of origin, there remains such a wealth of information of general interest that it deserves to be available to a much wider circle of readers.

Diagnostic Experimental des Helminthoses Animales. JACQUES EUZEBY. Vigot Freres, Paris. Fr. 2,605.

It is a commonly voiced criticism that the teaching of Veterinary Helminthology is too much concerned with morphology and taxonomy. Certainly, the student may well feel that he is unduly preoccupied with preserved specimens and diagrammatic representations of scolices, caudal bursae or other grotesque forms which might feel at home in a landscape by Salvador Dali but which appear quite as unrelated to the problems of diagnosing helminthic disease. The need for a treatise on the laboratory methods used in diagnosis has been acutely felt for many years, indeed the only satisfactory way in which the serious student could make himself familiar with these techniques appears to have been by visiting one of a small number of laboratories. This need Dr. Euzéby has attempted to fill. The layout of his book is good. In an admirably methodical fashion he deals with methods for the examination of faeces, urine, blood and skin, host animal by host animal, in each case discussing the details and relative merits of different techniques and the methods of identifying the eggs and larvae which they reveal. The recovery, examination and identification of helminths from different organs and tissues of the carcases of different hosts is dealt with in a similarly systematic manner. The keys, though deliberately oversimplified and occasionally unconventional are useful. A third section deals rather briefly with immunological methods. Sections on pseudoparasites, bodies of non parasitic origin which can be mistaken for helminth eggs or larvae are a valuable feature.

The principal defect of the book lies in the illustrations. It is not that these are insufficient in number, indeed they are so plentiful that when one encounters photographs of five beakers on a table or of two dishes, the one marked creasote and the other lactophenol, one is inclined to wonder whether the publishers have not erred on the side of generosity. It is the nature of the illustrations which is open to criticism. The problem which most commonly confronts the non-specialist is that of deciding to which of a small number of possible species a given specimen belongs. To achieve this quickly he can be very greatly assisted by good drawings. These should be drawn in a uniform style and to the same scale if they are to be truly comparable. Perhaps they should resemble caricatures rather than diagrams or lifelike representations and should stress those features by which one species may be distinguished from another. It is here that Dr. Euzéby has missed his opportunity. His readers must work from indiscriminately mixed collections of indifferent photographs at different magnifications and drawings and diagrams in a variety of styles and reproduced from a variety of sources. It is primarily this shortcoming that makes the contemplation of this book a distressing experience for it compares so unfavourably with the masterpiece that it might have been.

Lecture Outline of Preventive Veterinary Medicine for Animal Science Students. By I. A. SCHIPPER. Burgess Publishing Co., Minnesota. 18s.

As the title suggests, this book presents an outline of the material which is normally conveyed to agricultural students through the medium of formal lectures. In its brief form it is meant to serve as a basis to the lectures themselves and requires the complementary annotation and application of thought by the student to be of full value.

The first of the 9 chapters deals in elementary manner with principles of biology, anatomy and bacteriology, emphasis being placed on those aspects particularly concerned in preventive medicine. In the following pages more detailed information is given about the physiology and pathology of the various body systems as well as the medical aspects of the associated diseases commonly encountered in America. One chapter is devoted to the acute generalised infectious diseases not classified by anatomical systems, and parasitological conditions are dealt with separately. The book is on the whole very practical and will appeal to veterinary students as well as agricultural students.

The author expresses the hope that the outline of lectures "will aid the student to comprehend the normal physiologic functions of the domestic animals and to avoid the pitfalls of promiscuous medication. In addition it is hoped that the student will comprehend the value and need of competent veterinary service and the comprehensive training required to provide such service to the livestock industry."

A very full and useful glossary of terms is appended and the index of main subject matter is adequate. The paper covers and spiral-ring binding may not be durable but this style of presentation no doubt enables the book to be published at a reasonable price.

REPORTS

Food Investigation, 1957. The Report of the Food Investigation Board with the Reports of the Superintendents of the Torry Research Station, Low Temperature Research Station and the Ditton Laboratory. H.M. Stationery Office. Pp. 81. 5s.

The major part of this publication deals with research concerning the quality, freezing, cold storage, drying, curing, smoking, and canning of fish and the bacteriological and the biochemical aspects of these processes.

The rest of the work mainly deals with plant pro-

ducts such as vegetables and fruit and the problems involved in their storage and marketing.

Eight pages only are devoted to farm animal products, though many of these pages contain information of interest to those concerned with slaughtering and the wider aspects of meat inspection. Quality of fresh meat and offal, the bacterial flora of bacon, muscle physiology, and biochemistry are amongst the subjects dealt with. Statistically significant differences were found in the *p*H of the muscles of sugar-fed pigs. Such feeding appeared to have a marked effect on the growth rate of certain bacteria—particularly micrococci which are found on bacon and which have a practical bearing on the keeping quality. Preslaughter treatment of cattle with a view to increasing the ultimate muscle *p*H and with a view to decreasing the "drip" in frozen beef were investigated. No evidence was obtained that carcase weight was appreciably affected by detention of animals for 24 or even 48 hours in slaughterhouse lairages, although some liver wastage did result. Studies on *rigor mortis* have been continued with particular reference to the muscle relaxing factor, which operates in the presence of ATP (adenosine triphosphate). The strength of egg shells, the growth of bacteria within eggs, and the destruction of Salmonellae in egg products also receive mention. It is concluded that gamma radiation would provide a suitable method for the destruction of Salmonellae and other micro-organisms in liquid or frozen whole egg within the large tins in which these commodities are imported—without the necessity of thawing, pasteurising, and refreezing.

In the chairman's preface to the report, it is stated, "we regret that there are as yet no obvious signs of progress towards the provision of facilities for meat research in close association with an abattoir"—a sentiment which will receive hearty support from members of the British Veterinary Association.

H. E. B.

Canada Department of Agriculture: Report of the Veterinary Director-General for the Year ended March 31st, 1957.

The Health of Animals Division of the Canada Department of Agriculture consists of two sections; one is responsible for preventing and controlling contagious diseases of livestock, and the other for operating the Meat and Canned Foods Act and running the Canadian meat inspection service. In this Report, which is introduced by the veterinary director-general, Mr. K. F. Wells, concise informative accounts, supported by admirable statistics, of the activities of the two sections are given by their respective chief veterinarians. The whole Report is an interesting, lucid and readable document, from which it is clear that despite a continued shortage of veterinarians in the Division a very satisfactory position was maintained.

Mr. Wells rightly points out that one of the most important but least known functions of the Division is the import inspection of livestock and products capable of introducing animal diseases into Canada. This work is of course an integral part of disease control. During the year nearly 60,000 shipments including livestock products and agricultural products, were examined by divisional officers, and over 15,000 foreign ships and aircraft were checked for garbage and unauthorised uncooked meat.

Contagious Diseases Section. No new serious animal diseases gained entrance to Canada during the year. One of the most interesting tables in the Report is that showing the progress made in eradicating animal contagious diseases. Dourine, which at one time seriously threatened the Canadian horse-breeding industry, was eradicated in 1919 and glanders in 1938. Other diseases at times present in the country but which at the date of the Report had been absent for one or more years included sheep scab (last reported 1927), foot-and-mouth disease (1952), swine fever (1954), anthrax (1956) and horse mange (1956). Fowl pest has never occurred in Canada.

Progress was maintained in the plan for the elimination of bovine tuberculosis, and during the year the province of British Columbia was added to those in which all the cattle have been tuberculin tested. All areas except small parts of Alberta, Saskatchewan and Newfoundland have been submitted to tests at least once, and 90 per cent. of all the cattle in Canada, estimated at nearly 10,500,000 head, have been tested. In the 2,100,000 tuberculin tests conducted during the year only 0·13 per cent. reactors were uncovered, an average of 4 reactors to every 3,000 cattle tested.

Brucellosis has long been of economic importance to the country's cattle industry, but since 1947 control has been attempted under a Brucellosis-Free Listed Herd Plan which provides for official blood testing, removal of reactors and calfhood vaccination with S19 vaccine. It is a voluntary, individual herd policy. At the close of the year 3,454 herds, involving 117,900 cattle, were receiving attention, of which 2,959 herds were listed free. In addition to this scheme for freeing herd infection, another plan provides for calfhood vaccination to facilitate movement of young stock to shows, fairs and sales; nearly 774,000 calves were vaccinated during the year, an increase on the previous year's figures. Plans were also in hand for the early inauguration of a programme to control and eradicate contagious abortion on an area basis.

The position in regard to rabies was less satisfactory; judged on the number of confirmed cases the incidence of the disease has been higher during the past 3 years than ever before. During the year under review 179 cases, most of them in Quebec and Ontario provinces, were detected; 105 were in foxes, 9 in dogs and the rest in other animals. No human fatalities were reported. Counter measures included control of dog movements and the establishment of free vaccination clinics. Approximately 15,000 dogs were vaccinated.

The incidence of Newcastle disease continued to decrease and although 18 outbreaks occurred it was not deemed necessary to invoke the slaughter policy, control being achieved instead by vaccination. Appropriate measures are taken against introduction of the disease through imported live poultry, hatching eggs, crates and vehicles. Thirty-four cases of fowl typhoid were also dealt with by the Division.

Chorioptic mange in cattle was detected on 22 premises. The herds were quarantined and the cattle treated under official supervision. No sarcoptic or psoroptic mange was reported. Scrapie was identified on two premises.

Other activities of the Contagious Diseases Section included control of the feeding of garbage to prevent swine fever and poultry diseases, the disinfection of cars and trucks carrying stock and poultry, the licensing of the importation, manufacture, sale and use of all veterinary biologics, and the enforcement of regulations to prevent the introduction of diseases through semen imported for breeding.

Meat Inspection Section. This section fulfilled a very important function in its maintenance of the meat inspection service, a service which completed its 50th anniversary during the year. Regular *ante-* and *post-mortem* inspections were conducted at 104 slaughtering and 57 meat-processing establishments during the year, supported when necessary by analyses and bacteriological examinations, to ensure that meat and meat products, including poultry, whether for local consumption or for export, were of the highest quality and safety. Over 24,000,000 head of livestock and poultry were inspected during 1957, an increase of over 40 per cent. on the previous year.

The report on this section contains very comprehensive statistics, including a full list of the pathological conditions encountered during inspection. It is interesting to note that in addition to relatively large imports of fresh and canned meats into Canada from the U.S.A. sizeable quantities were also received from Australia and New Zealand.

W. E. L.

News and Comment

INCOME TAX RELIEF ON B.V.A. SUBSCRIPTIONS

As will be seen from the letter below, the Commissioners of Inland Revenue have approved the British Veterinary Association for the purposes of Section 16 of the Finance Act, 1958. As a result, the whole of the annual subscription paid by a member who qualifies for relief under this Section will, commencing in 1959, be allowable as a deduction from his emoluments assessable to income tax under Schedule E.

A member of the Association who is entitled to this relief should apply to his tax office as soon as possible for form P358 on which to make a claim for adjustment of his P.A.Y.E. coding.

Communications on this subject should be addressed direct to the member's local tax office.

The following is the letter received from the Inland Revenue:—

Inland Revenue (Chief Inspector of Taxes Branch),
New Wing, Somerset House, London, W.C.2.
Ref. C.I/SUB/163.

2nd April, 1959.

Dear Sir,

I have to inform you that the Commissioners of Inland Revenue have approved the British Veterinary Association for the purposes of Section 16, Finance Act, 1958, and that the whole of the annual subscription paid by a member who qualifies for relief under that Section will be allowable as a deduction from his emoluments assessable to income tax under Schedule E. If any material relevant change in the circumstances of the society should occur in the future you are requested to notify this office.

I should be glad if you would inform your members as soon as possible of the approval of the society. The circumstances and manner in which they may make claims to income relief are described in the following paragraphs, the substance of which you may care to pass on to your members.

Commencing with the year to 5th April, 1959, a member who is assessable to income tax under Schedule E in respect of the emoluments of an office or employment is entitled to a deduction from those emoluments of the whole of the annual subscription which is due and payable by him to the society in the income tax year *provided that:—*

(a) the subscription is defrayed out of the emoluments of the office or employment, and,

(b) the activities of the society so far as they are directed to all or any of the following objects:—

(i) the advancement or spreading of knowledge (whether generally or among persons belonging to the same or similar professions or occupying the same or similar positions);

(ii) the maintenance or improvement of standards of conduct and competence among the members of any profession;

(iii) the indemnification or protection of members of any profession against claims in respect of liabilities incurred by them in the exercise of their profession; are relevant to the office or employment, that is to say, the performance of the duties of the office or employment is directly affected by the knowledge concerned or involves the exercise of the profession concerned.

A member of the society who is entitled to the relief should apply to his tax office as soon as possible for form P358 on which to make a claim for adjustment of his pay as you earn coding.

Yours faithfully,
Signed, W. Walne,
Senior Principal Inspector of Taxes.

The General Secretary,
British Veterinary Association.

Readers may like to be reminded that Section 16 of the 1958 Finance Act, together with the fifth schedule of that Act, makes the annual fee payable to the Royal College of Veterinary Surgeons a proper deduction, in the words of the Act, "from the emoluments of any office or employment to be assessed to tax if defrayed out of those emoluments." That is to say R.C.V.S. fees may now be set against income tax by *all* members, instead of only by members paying their tax under Schedule D.

THE FITZWYGRAM, WILLIAMS, WALLEY AND LAWSON PRIZES—1959 GRADUATES

The Prize Board gives notice that the subject selected for the essay competition—open to candidates who obtain a registrable qualification in the calendar year 1959—is "Review of the Problem of Strongylosis in the Horse, Ox, Sheep, and Pig."

Intending candidates are referred to the regulations for the prizes on pages 531 and 532 of the Register of Veterinary Surgeons for 1958, and any further information may be obtained from the Registrar of the R.C.V.S.

At a meeting of the Council of the Royal College on June 12th, 1958, it was resolved that in the case of those persons who passed their examinations in December or in earlier months, but who were not formally admitted to their degrees until January or later months, they should be regarded as candidates for the prizes which fell within the year in which they passed their final examinations.

WELLCOME VETERINARY RESEARCH FELLOWSHIPS

Applications are invited by the the Animal Health Trust for the appointment of a Wellcome Fellow for whole-time research in connexion with veterinary science or medicine, from any person who on October 1st, 1959, is under 36 years of age and holds the Membership Diploma of the Royal College of Veterinary Surgeons or a degree in any faculty relevant to veterinary science or medicine in any university in the British Commonwealth and Empire. Applicants are expected to have done some post-graduate work and to provide evidence that they have been able to make arrangements for the satisfactory conduct of the proposed research.

A Fellowship may be awarded at an annual value of £850 rising by annual increments of £50. The Fellowship is subject to income tax and carries benefits under the F.S.S.U.; it is tenable for one year in the first instance and by annual reappointment for a further period of 2 years at the discretion of the Advisory Committee. Election will be made in June, to take effect as from October 1st, 1959. The closing date for receipt of applications is Thursday, April 30th.

Forms of application are obtainable from: The Scientific Director, The Animal Health Trust, 14, Ashley Place, Westminster, London, S.W.1.

A.V.M.A. PRESIDENT-ELECT TO ATTEND R.C.V.S. DAY

The American Veterinary Medical Association has nominated its President-elect, Dr. S. F. Scheidy, of the University of Pennsylvania, and veterinary medical director of the firm of Messrs. Smith Kline and French Laboratories Limited, to be its official representative at R.C.V.S. Day on June 2nd.

The President-elect has accepted an invitation from the President of the Royal College to be a principal speaker and will respond to the toast of "The Guests" at the College luncheon.

Tickets and particulars regarding all the ceremonies of R.C.V.S. Day may be obtained from the Registrar, 9, Red Lion Square, London, W.C.1.

EXHIBITIONS AT THE INTERNATIONAL VETERINARY CONGRESS

The Congress will include exhibitions of industrial and scientific materials and it is expected that most or all of the countries who are sending delegates will be represented. These at present include the United States, South America, France, Belgium, Italy, the U.S.S.R., Japan, Portugal, the Netherlands, Turkey, and Great Britain. Interest in the scientific and commercial exhibitions has also been shown by West Germany, Sweden, and Switzerland.

We understand that the Spanish customs authorities will permit temporary entry free of duty of the materials which are to be exhibited. The exhibitions themselves will be housed in a large hall within the main Congress building.

MR. H. A. SCOTT DUNN

Mr. A. G. Welch writes:—

In my college days, if Brighton was mentioned, the name of Scott Dunn automatically came to mind. When I eventually found myself living in Brighton, "Scottie," was the first colleague to call and extend a welcome, insisting on nominating me for the B.V.A. and being generally helpful. I have seen him do the same for other newcomers since, and "kind" and "helpful" are the two characteristics I shall always associate with "Scottie."

He soon became a friend, and his brief but cheery visits will be greatly missed both by my wife and by myself.

THE FIRST JEPHCOTT LECTURE

The first lecture arranged by the Jephcott Lectures Trust will be entitled "Nucleic Acids and their Rôle in Future Chemotherapy of Tumours and Virus Diseases." It will be delivered by Sir Alexander R. Todd, Professor of Organic Chemistry in the University of Cambridge, at the Royal Society of Medicine, 1, Wimpole Street, London, W.1, at 7 p.m. on Wednesday, May 27th, 1959. Admission will be by ticket only, and application for tickets may be made to The Secretary, The Jephcott Lectures Trust, 1, Carlos Place, W.1.

THE SUSSEX VETERINARY SOCIETY

A party of members of the Sussex Veterinary Society and their friends decided to pay a visit to the 68th General Agricultural Show in Paris, for the purpose (among others) of acquainting themselves with the points of the Charollais breed.

Leaving Croydon aerodrome in a chartered Heron on Saturday morning, March 21st, they were in the Show by 2 p.m. and spent a most enjoyable afternoon looking at some of the famous French breeds of cattle, horses, and sheep.

Sunday morning was spent in sightseeing, and the party returned to Croydon in the early evening well pleased with their excursion.

XUM

HOLIDAY EXCHANGES

France

Girls. Martine Bardonneche, aged 16, of the Hautes-Alpes region in the south-east of France, would like to arrange an exchange holiday in England for 1 month.

A 12-year-old French girl would like to correspond with another girl in this country with a view to arranging an exchange during the summer holidays. The family live near Angers in the west of France, not far from the sea.

Marie-Claude Bru, aged 15, would also like to arrange an exchange holiday. She would like to stay with a family on the south coast, if possible, as she is interested in swimming, tennis, and horse riding. Her home is in Esternay (Marne), and she hopes to come to England for a period of 3 weeks to a month.

Mlle Delton of Sainte-Sévère (Indre), aged 16, would like to exchange with a girl of her own age living in or near London.

Michère Ducom of the Sarthe region in the west of France is also anxious to come to England: she is aged 15, and has no particular preference for any part of the country. Mlle Metayer, aged 15, who lives in a small town in Vendée in the western part of France, also hopes to come to England under the same terms.

Edith and Anne-Marie Mignolet, aged 15 and 16, respectively, hope to arrange a stay of 1 month in England during the summer; they would then return to France with their hosts for an exchange holiday in a village in the Loire-Atlantique region of France.

Boys. Bernard Frey, aged 14, of Rheims, would like to come to London for about 1 month during July or August, the details of the exchange to be worked out by the families concerned.

Yves Labruyere, aged 16½, is anxious to contact a boy of his own age with a view to arranging an exchange holiday of 15 days to 3 weeks. He would like to correspond about this as soon as possible. He lives in the Pas de Calais region of France.

Paying Guest. A French veterinary family would like to arrange for their son, aged 13½, to stay with an English veterinary family as a paying guest during the summer months.

Au Pair. A French veterinary family offers a room to an English girl in Paris in exchange for English lessons. It would be possible for the girl to stay for several weeks or several months, as she wished.

Germany

A young German student, aged 19, intending to study veterinary science, would like to help an English veterinarian during the July holidays. He does not require any remuneration but would give his services in exchange for hospitality. If any veterinary surgeon is interested perhaps he would communicate direct with Mr. Hans-Christian Hillscher, whose address is 22a, Krefeld-Hülserberg, Rennstieg 15, Germany.

Dr. Meyer of Westerhausen would like to arrange an exchange visit for his 15-year-old son, the English boy to visit Germany in the summer holidays of this year and his own son to make the return visit in 1960.

Members of the profession who may be interested in contacting any of the families listed above are asked to address their enquiries to the Editorial Department of THE VETERINARY RECORD.

THE REGISTER OF VETERINARY SURGEONS

The undermentioned gentlemen were admitted to the Commonwealth List of the Register of Veterinary Surgeons on March 31st, 1959: Hellig, Howard, B.V.SC. (PRETORIA), c/o South Africa House, Trafalgar Square, S.W.1, and Worthington, Robert Walter, B.V.SC. (PRETORIA), c/o South Africa House, Trafalgar Square, S.W.1.

The name of Portway, Bruce, B.V.SC. (SYDNEY), M.V.SC. (TORONTO), c/o National Bank of Australasia, Australia House, London, W.C.2, was entered on the Commonwealth List of the Register on April 6th, 1959.

UNIVERSITY NEWS

Liverpool

At its meeting on March 17th, 1959, the Council of the University approved the appointment, as from October 1st, 1959, of Mr. J. McC. Howell, B.V.SC., M.R.C.V.S., as lecturer in veterinary pathology.

MR. JOHN WILLIAMS NICHOLAS

Captain Ivor Hughes writes:—

It is with deep regret that I refer to the death of the President of the Supplementary Veterinary Register Division of the B.V.A., Mr. J. W. Nicholas. His sudden passing came as a great shock to all those who knew him. He was a founder member of our Division, and had filled the office of President since its inception. I know that every member would witness to his great ability, and his personal kindness. Each of us, as well as the Division as a whole, has lost a real friend who will not be easily replaced.

I shall miss him sorely, and feel, like all my colleagues, the poorer for his passing. The well-being of the Division was very close to his heart, and none knew that better, from personal experience, than I having worked at his side as the S.V.R. Division's honorary secretary. May I offer the condolences of all our members to his family.

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The funeral took place on Friday of last week at the South-west Middlesex crematorium, and the British Veterinary Association was represented by its honorary treasurer, Dr. E. Cotchin.

R.C.V.S. OBITUARY

We record with regret the deaths of the following members of the profession:—

DUNN, Herbert Anderson Scott, of Benfield House, Hangleton, Hove, Sussex. Graduated Edinburgh, December 16th, 1907. Died April 2nd, 1959, aged 74 years.

NICHOLSON, Edward, The Thatched Cottage, Stowe Road, Purleigh, Essex, Captain R.A.V.C. (Retd.). Graduated December 18th, 1900, at the Royal Veterinary College, London. Died March 24th, 1959.

Supplementary Veterinary Register

NICHOLAS, John Williams, 62, Park Road, Hounslow, Middlesex. Admitted to the Register December 23rd, 1949; died March 31st, 1959.

PERSONAL

Mr. H. D. Dewar, veterinary officer of the Animal Health Division who was stationed at Dorchester, has resigned.

Mr. Peter Robert Kemble, a veterinary student, of Nuneaton, was presented with the Royal Humane Society's Life Saving Certificate at the Nuneaton Magistrates Court last week. He saved a nine-year-old boy from drowning.

Mr. W. J. Sojka, of the Ministry's laboratory at Weybridge, will be visiting the International Salmonella and Escherichia Centre, State Serum Institute, Copenhagen, for a month starting April 26th, to study the typing methods and recent developments in this field.

Marriage

O'BRIEN—PICKIN.—On April 4th, 1959, at St. Joseph's Church, Sheffield, James O'Brien, M.R.C.V.S., of Woodhouse, Sheffield, to Valerie Pickin of Dore, Sheffield.

Birth

CRIBB.—On March 26th, 1959, to Marigold, wife of Peter H. Cribb, B.SC., M.R.C.V.S., of 59, King Edward Road, Thorne, Yorks, a daughter.

EVANS.—On March 29th, 1959, at the County Maternity Home, Aberystwyth, to Mair, wife of T. D. Evans, M.R.C.V.S., of Tegwil, Banadl Road, Aberystwyth, a daughter.

FORD.—On April 5th, 1959, to Rosalind, wife of M. P. Ford, B.SC., M.R.C.V.S., of Star Lock, Playden, Nr. Rye, Sussex, a daughter, Sara Kathleen.

HENDERSON.—At Rio de Janeiro, on March 8th, 1959, to Beryl, wife of Dr. W. M. Henderson, Pan American Foot-and-Mouth Disease Center, a son.

COMING EVENTS

April

15th (Wed.). Meeting of the Warwickshire Veterinary Club in the Regent Hotel, Leamington Spa, 8 p.m.

16th (Thurs.). Meeting of the Herts. and Beds. Veterinary Society at the George Hotel, Luton, 7.30 p.m.

Annual General Meeting of the Lakeland Veterinary Association at the Nag's Head, Kendal, 7 p.m.

17th (Fri.). Meeting of the Yorkshire Veterinary Society at the Hotel Metropole, Leeds, 2.30 p.m.

22nd (Wed.). Ordinary General Meeting of the Southern Counties Veterinary Society at the Polygon Hotel, Southampton, 7.30 p.m.

25th (Sat.). Meeting of the B.S.A.V.A. North West Region at the Stork Hotel, Liverpool.

Annual General Meeting of the Association of State Veterinary Officers in the Auditorium of the Wellcome Research Institute, 183-193, Euston Road, London, N.W.1, 4 p.m.

May

1st (Fri.). Reception and Dance of the Midland Counties Veterinary Association at the Mount Hotel, Tetterhall Wood, Wolverhampton, 9 p.m.

August

30th to 5th September. 77th Annual Congress of the British Veterinary Association in Folkestone. (Official opening Monday, August 31st.)

ADDRESSES OF DISEASE INFECTED PREMISES

The list given below indicates, first the county in which are situated the premises on which disease has been confirmed, followed by the postal address and date of outbreak.

Anthrax

Dumfries. Drummuir Farm, Collin; Croftjane, Thornhill (Mar. 31).
Perth. Moneydie Farm, Luncarby (Mar. 31).
Staffs. Longacre Farm, Buthbury, Rugeley (Mar. 31).
Stirling. Blairmains Farm, Blairlogie (Apr. 2).
Suffolk. Valley Farm, Boyton, Woodbridge (Apr. 2).

Fowl Pest

Bucks. Fourtrees, Mill Lane, Amersham (Apr. 2).
Derby. Plough Inn, Two Dales, Matlock (Apr. 1).
Dorset. 4, Hambro Terrace, Preston, Weymouth (Apr. 1).
Essex. Shirley, Lower Park Road, Wickford (Apr. 1); Ayletts Farm, Halstead (Apr. 2).
Herts. 69, Queens Road, Hertford (Mar. 31); 2, Downfield Road, Hertford Heath (Apr. 2).
Surrey. Rowlands Farm, Lingfield (Apr. 1).

Swine Fever

Berks. Warren Farm, Streatley, Reading (Apr. 1).
Bucks. White House Farm, Bourton (Mar. 31); Love Hill Farm, Love Hill Lane, Langley, Slough (Apr. 2).
Ches. Home Farm, Puddington, Wirral (Apr. 1).
Essex. Berechurch Poultry Farm, Kingsford, Berechurch, Colchester (Mar. 31).
Flints. Griana, Babell, Holywell (Apr. 2).
Gloucs. Poulton Farm, Blakeney (Apr. 1); Mussleland Farm, Sandhurst (Apr. 2).
Salop. Moss Side, Bankhouse Lane, Wem, Shrewsbury (Apr. 1); Grafton Farm, Montford Bridge, Shrewsbury (Apr. 2).
Warwicks. Harrow Hill Farm, Long Compton, Shipston on Stour (Mar. 31); Stepmoles Farm, Halford, Shipston on Stour (Apr. 1).
Wilts. Halfway Farm, Beanacre, Melksham; Inwood Lacock, Chippenham (Mar. 31).
Worcs. St. Huberts, Hadzor, Droitwich (Apr. 1); Sinton Farm, Grimley (Apr. 2).

ADVERTISER'S ANNOUNCEMENT

GLAXO LABORATORIES LTD. announce the introduction of the following new Canine Vaccines from Monday, April 6th:—

Dual Canilin, containing one vial freeze-dried Canine Distemper Vaccine, one ampoule sterile distilled water and two ampoules Canine Virus Hepatitis Vaccine in a single patient pack.

Canilin-D, containing one vial Canine Distemper Vaccine plus one ampoule sterile distilled water.

Canilin-H, containing two ampoules of killed Canine Virus Hepatitis Vaccine—a single patient pack.

Lepsolin, containing 2 × 2 ml. ampoules of combined *L. canicola* and *L. icterohaemorrhagiae* vaccine— single patient pack.

Also announced is: the introduction of a mixed enterotoxaemia vaccine (March 31st). This vaccine is for the protection of sheep against enterotoxaemia caused by *Clostridium welchii* types C and D.

Price reductions for veterinary packs of Predsolan and Cytamen came into effect from Monday, April 6th.

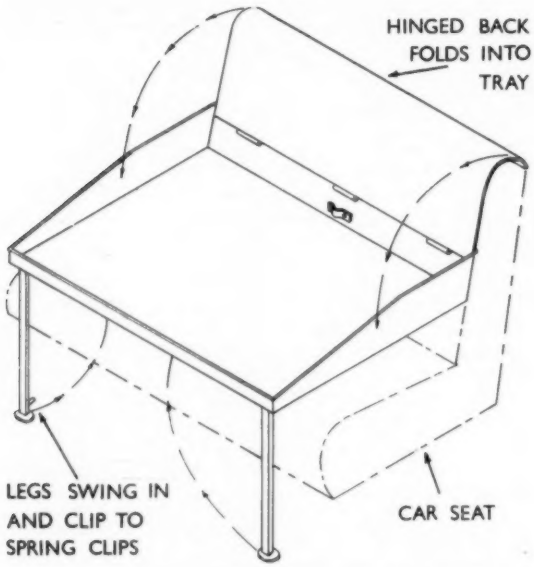
Letters to the Editor

The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.

A Useful Car Fitment

Sir,—Attached to this letter is my design for a tray which can be inserted into the back of a saloon car and used for the carriage of small animals. It is not unduly heavy and can be inserted into, or removed from, the car in about a minute.

No weight is taken by the rear seat proper—the tray being slung from the top of the rear seat. Wear is thus avoided.



The trays I have in use are made of galvanised iron and are, of course, rust-proof and leak-proof. I find them particularly useful in the avoidance of contamination of the car during carriage of cats, etc.

Messrs. Cope & Cope of Reading hold a copy of the design, and would no doubt manufacture trays to the requirements of members of the profession.

Yours faithfully,
W. J. McCORMICK.

113, Oxford Road,
Reading.
March 23rd, 1959.

Salaries in the Veterinary College of Ireland

Sir,—May I take this opportunity, through the courtesy of your colums, to support the plea of Mr. Esmonde Little (*Vet. Rec.* **71**. 245) for adequate, even generous, salaries for the veterinary surgeons employed by the Irish Minister for Agriculture?

Apart from the eradication of hog cholera which he mentions, these gentlemen have also eradicated fowl pest from their country. Their success in these endeavours is an object lesson which should be taken to heart by the politicians and bureaucrats who are concerned with animal disease control in Great Britain. These achievements are all the more remarkable inasmuch as they have been accomplished in a country whose resources in finance and man-power are so much less than those of Great Britain.

His reference to the Slaughter of Calves Order is also very interesting, and it is but one example of the futility of politicians failing to take advice from their own veterinary experts. In Great Britain, for example, we have seen the importation of fowl pest from Hungary when Mr. J. Strachey was Minister of Food, and also the continuing importation of foot-and-mouth disease from Argentina by successive British Governments of both political persuasions. Furthermore, the politicians and bureaucrats will continue to inflict their fatuous decisions upon the veterinary profession and livestock industry, until such time as the veterinarians and livestock owners in the countries concerned consult together with a view to exerting the necessary political pressure upon their parliamentary representatives.

I wish the Irish V.M.A. well in their efforts to obtain fair treatment for veterinarians in the service of the Minister for Agriculture. They deserve the fullest possible support from the B.V.A. and R.C.V.S.

Yours faithfully,
J. N. SIMPSON-WHITE.

9629, San Luis Avenue,
South Gate,
California,
U.S.A.
March 30th, 1959.

Some Nutritional and Other Interacting Factors which may Influence the Fertility of Cattle

Sir,—I should like to draw attention to the fact that, in the paper "Some Nutritional and Other Inter-acting Factors which may Influence the Fertility of Cattle," published in THE VETERINARY RECORD on March 28th, the x_1 values shown in Figs. 1, 2, and 3 are wrongly placed. To obtain proportional spread, logarithmic paper (linear log 1 cycle) was used in the original plotting from which these figures were evolved. Consequently, the interval between two consecutive whole numbers becomes smaller in passing from left to right. The 0 should appear under the left hand corner; 0.5 at the junction between areas A and B; 1.0 between G and H; 2.0 between H and J; and 3.75 between B and C. The boundaries of these areas are, in fact, given in full in the left-hand column of page 248.

I should be very grateful if these corrections could be brought to the notice of your readers.

Yours faithfully,
S. L. HIGNETT.

The Wellcome Veterinary Research Station,
Frant,
Tunbridge Wells.
April 3rd, 1959.